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Treatment of Schizophrenia*

An Experimental Study of Five Treatment Methods

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The clinician is deeply concerned with the difficulties of selecting a treatment method that will accomplish the goals which he wishes to achieve for a particular patient with specific symptoms and characteristics in a particular treatment setting, knowing that it is unlikely that any one single treatment will be universally and equally effective in all situations. The research investigator should attempt to help him by furnishing objective evidence as to the specific efficacies and limitations of methods of treatment in common use under the conditions that prevail where large numbers of patients are treated—in public mental hospitals. Adequate comparative information obtained under controlled experimental conditions is essential not only to therapists but also to patients and their families and to those responsible for the support and administration of treatment centres.

In the absence of a universally accepted definitive treatment for schizophrenia, and faced with a wide difference of opinion about the relative efficacy of new and old methods of treatment, the clinician and the administrator find that their choice of treatment is often influenced, if not entirely by sheer prejudice, at least to a large extent by the availability of one or another treatment method, rather than by the weight of evidence for its appropriateness and effectiveness. Individual psychotherapy in a public hospital setting, for instance, may appear to be a costly enterprise. If there is a severe shortage of trained personnel, or of proper supervision, it may be avoided in preference to milieu therapy, social therapy, drug treatment or electroshock—whichever happens to be more readily available or more in keeping with the fashion of the moment. In another setting, however, a patient may be given individual psychotherapy for a long period of time, not because there is overwhelming scientific evidence that psychotherapy is the only treatment that is likely to be effective for this particular patient, but rather because there is insufficient scientific evidence to establish acceptable limits or guidelines to direct the enthusiasm and technical skills of the therapist and the resources of the institution.

There is considerable debate about the appropriateness of psychotherapy for schizophrenic patients; about the long range value of electroshock or drug therapy; about the alleged facilitating or inhibiting effects of pharmacological agents on the psychotherapeutic process; and about the "sufficiency" of physical treatment in any form for an illness that is thought to have its aetiology, at least in part, in psychological events. Such controversies will undoubtedly continue until specific tested evidence can replace the ignorance, convenience, bias, traditional routine and other irrational elements that now enter into and influence our present decisions in the selection of treatment.

Design of the Study

Forty-seven male and fifty-three female schizophrenic patients were selected from con-

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secutive admissions to Camarillo State Hospital between July, 1959 and March, 1961, the selection being carried out by three teams of two psychoanalysts each meeting on a separate day of the week. We wished to study those patients where treatment might make the greatest difference between success and failure. Accordingly, using the principle of "triage", patients were excluded if, in clinical judgment, they were considered to have little chance of leaving the hospital in less than two years, or if they were already restituting during the initial evaluation period (average 18 days). These clinical intuitive judgments, made mainly on the basis of length of illness and indications of chronicity, seem to have been reasonably successful in selecting out the desired range—for the entire sample, including treatment failures, the mean hospital stay was 210·4 days with a range of 36–688 days.

It should be noted particularly that we were studying the *middle section* of the prognostic range. This does provide some rational basis for assuming that the results may be somewhere near the median for the entire prognostic range. However, it is possible that different treatment tactics may be applicable to patients who may perhaps leave the hospital rapidly regardless of the treatment given; or at the other extreme to those patients who may perhaps become chronic in any case. The reader is, therefore, cautioned against over generalizing too glibly from the results of this study to the treatment of these other prognostic sectors.

After selection and initial evaluation, patients were assigned by a random method to one of five treatment methods—individual psychotherapy; drug therapy; individual psychotherapy plus drugs; electroshock therapy; and "basic care" or "control", which did not include any of the specific treatments listed above. Evaluation was carried out before and after treatment using multiple independent criteria. Table I shows that the five groups were satisfactorily equated in terms of sex, age, race, education, occupation, religion and initial level of illness as gauged by the Menninger Health-Sickness Rating Scale (Luborsky (1)). Therefore, there is no reason to believe that the patients in the five treatment groups are not homogeneous or do not come from the same population. The "average" patient was 27 years old, semi-skilled and with an 11th grade education; had had predominantly paranoid psychotic symptoms for an average of 23 weeks and was not entering the hospital voluntarily. The group included patients who were assaultive, suicidal, mute or greatly disorganized in their behaviour.

Treatment

The treatment setting is a 6,000 bed State Hospital located in a relatively rural community in Southern California, some 50 miles northwest of the City of Los Angeles. The study patients were housed in a 20-bed male and a corresponding 20-bed female ward with an individual room for each patient, with similar architecture, physical facilities, staffing, ward programme and organized activities. The basic programme of care provided for all treatment groups included nursing care, sedation, hydrotherapy, occupational, industrial and recreational therapies, ward meetings and social casework.

The physicians who treated these patients were 14 male and 3 female residents in psychiatry or psychiatrists with less than five years of psychiatric experience, between the ages of 30 and 54 with an average age around 40 years. This, we estimate, corresponds in general with the level of experience of physicians who may be reasonably expected to be found to treat patients in state hospitals. Each patient's treatment was supervised by a senior psychiatric consultant who believed in the efficacy of the particular treatment method he supervised. The consultant and the patient's own physician were jointly responsible for all matters of timing, management, dosage, strategy, duration of treatment and other operational details. While the supervisors were, in a sense, specialists in one or another method of treatment and provided supervision on one specific method only, the therapists treated patients in all treatment groups.

Psychotherapy was given for an average of not less than two hours a week, supervised by a psychoanalyst experienced in the treatment of

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TABLE I

*Patient Characteristics by Treatment Group**

	C	ECT	D	P	D&P
Sex:					
Male	11	10	11	10	11
Female	9	10	9	10	9
Age:					
Mean	27·1	29·6	27·9	25·5	27·6
Standard deviation	5·9	4·9	4·1	5·6	7·4
Race:					
White	14	15	13	11	14
Negro	4	2	5	4	3
Other	2	3	2	5	3
Education:					
Partial College or more	4	5	4	7	4
High School	10	7	9	7	8
Not completed High School	6	8	7	6	8
Occupation:					
Unskilled	1	2	4	2	1
Semi-skilled	3	3	2	3	6
Skilled	3	3	1	1	1
Clerical or above	7	5	5	6	8
Religion:					
None	2	3	4	1	2
Protestant	4	11	9	10	8
Catholic	11	5	6	8	8
Jewish	2	0	–	–	1
Other	1	1	1	1	1
Initial Menninger Health-Sickness Rating					
Mean	19·5	19·0	19·3	19·5	18·3
Standard deviation	4·0	2·8	4·5	3·6	4·0

* In this and in all other Tables, the following abbreviations are used for the different treatment groups: C=Control or basic care. D=Drug alone. P=Psychotherapy alone. ECT=Electroshock. D&P=Drug plus psychotherapy.

schizophrenic patients, with one hour of supervision for each patient every two weeks.

For patients treated with ataraxic drugs, the aim was to give whatever type or dose the supervisor judged most likely to be effective, to study treatment under "battlefield conditions" and *not* to conduct a study of a fixed dosage or of a particular drug. The main drug used was Stelazine, given orally, although intramuscular medication was given briefly to some uncooperative patients and a few received Thorazine (Largactil) concurrently. Kemadrin was given prophylactically and routinely as an anti-parkinson agent. The "drug alone" group, had a maximum daily dose of Stelazine averaging 25·5 mg. with a range of 10–40 mg., except for one patient who received up to 70 mg. The "drug plus psychotherapy" group had a maximum drug dosage averaging about 18·7 mg., somewhat lower than that of the "drug alone" group. Although drugs were gradually withdrawn as patients approached their release, some patients were discharged on maintenance dosage.

Electroshock treatment was generally given three times a week at the beginning, reduced to twice and then once a week if the patient showed gross signs of confusion and memory loss. The actual number and frequency of treatments was, in each case, decided by the therapist in consultation with the supervisor, treatment being maintained to maximum clinical improvement. The total number of treatments for each patient ranged from 10 to 48 with a mean of 22. A Dale machine was

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used, after intravenous administration of Thiopental and succinyl-choline.

The "control" group received no "specific" treatment, only the basic level of care described earlier, and which was equally available to patients in the other treatment groups.

For patients in all groups, treatment was continued up to a maximum of one year, unless the patient was released from hospital before that. Treatment could be abandoned as a "failure" if the patient had been on the treatment for at least six months *and* the supervisor and therapist agreed that it had been given a good trial and that further continuation with that particular method was unlikely to succeed.

Complications

There were no serious *medical* complications from any of the treatment methods. More outstanding were the *administrative* complications resulting from staff attitudes to random assignment of treatment and to maintaining patients on their original treatment for 6–12 months—particularly the control group who received no specific treatment. It will be readily understood that considerable thought, effort, time, patience and persistence were required for the implementation of the design and the maintenance of staff and patient morale over a three-year period. There were no major problems with patients' or their families' attitude toward the research project or towards any of the treatment methods.

Outcome Criteria

Previous reports from this study (May (2), May and Tuma (3, 4)) have considered separately the relative effectiveness of electroshock and tranquillizing drug; and of tranquillizing drug and psychotherapy, using four criteria of outcome: release rate from hospital, length of hospital stay, the amount of supplemental treatment (hydrotherapy and sedation) needed, and the estimated amount of global clinical change. The present report provides simultaneous comparison of all five treatment methods: it also utilizes four different criteria of outcome which are complementary to those reported earlier and yet have specific theoretical and practical significance. These criteria are:

1. Re-hospitalization rate during the two years after first release from hospital.
2. Total length of time (days) in hospital during a three-year period from the date of first hospitalization.
3. The patient's post-treatment status on the Menninger Health-Sickness rating scale (Luborsky (1)). The MHS is a 100 point clinical judgment scale of overall mental functioning with 34 case examples illustrating the different levels of health: "100" represents an ideal state of mental health, and "0" extreme sickness—a condition which if unattended would quickly result in the patient's death. Ratings were provided by eight psychoanalysts working in teams of two, the same team evaluating the patient before and after treatment, and recording their consensus ratings after discussion based on an interview, with the social and psychiatric histories and progress notes available to the raters. The raters were not actually told what treatment the patient had received, but since the psychoanalysts did a reasonably detailed unstructured interview, it would be safe to assume that the raters, although independent of the treatment and supervising staff, received in the course of the interview varying clues as to the actual treatment given.
4. The patient's ward behaviour at the end of treatment was rated on the MACC rating scale (Ellsworth (5)). This includes 14 items of ward behaviour, summed to give a total adjustment score. A research nurse recorded consensus ratings arrived at by discussion of the patient with two other members of the ward nursing staff.

Results

1. *Post-treatment Status—Menninger Scale*

The observed inter-group differences on this measure were examined for possible true differences by an analysis of variance. As is evident in Table II, the F test shows that the

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TABLE II

Post Treatment Status—Menninger Health–Sickness Scale

A.—Analysis of Variance

Source of Variation	d.f.	Mean Square	F
Between treatments	4	214·75	2·94*
Within treatments	95	72·97	
Total	99		

B.—Treatment Group Means Ranked in Order

C	P	ECT	D&P	D
26·15	28·95	29·1	33·55	33·75

NOTE: Any two means not underscored by the same line are significantly different (5 per cent. level test).
* $p<·025$.

observed differences are unlikely to be due to chance variation ($p<·025$).

Furthermore, examination of the group means by Duncan's New Multiple Range Test (Duncan (6)) demonstrates that the "drug" and the "drug plus psychotherapy" groups were rated significantly higher than the control group but that there were no other statistically significant differences between groups. An analysis of variance for the "control", "drug alone", "drug plus psychotherapy" and "psychotherapy alone" groups (Table III) reveals that the main effect is due to the drug treatment ($p<·005$) and that no significant effects could be attributed to the interaction between psychotherapy and drugs. (The analysis employed a 2×2 factorial design with one main factor drug and the other main factor psychotherapy.)

TABLE III

Source of Variance in Menninger Ratings: Four Treatment Groups Only

Source	d.f.	Mean Square	F
Drugs	1	744·2	9·85*
Psychotherapy	1	33·8	·44
Interaction	1	45·0	·59
Within treatments	76	75·53	
Total	79		

* $p<·005$.

2. *Post-treatment Status—MACC*

Table IV shows that the five treatment groups manifest mean differences in MACC total adjustment scores that cannot be readily explained as chance variation ($p<·001$). A New Multiple Range Test shows that the "drug" and "drug plus psychotherapy" groups had scores that were significantly higher than "electroshock", "psychotherapy alone" or "control".

Furthermore, Table IV shows that psychotherapy added to drug does not differ significantly from drug alone on this measure. Neither "electroshock" nor "psychotherapy" is significantly different from "basic care" alone ($p>·05$).

There are no other statistically significant differences, and analysis of variance, excluding the E.C.T. group (Table V), shows that the main effect can be attributed to the drug treatment alone ($p<·001$). (This analysis employed a 2×2 factorial design with one main factor drug and the other main factor psychotherapy.)

3. *Re-hospitalization*

Table VI shows for each of the five treatment groups, the number of patients re-admitted to

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TABLE IV

Post-Treatment Status—MACC

A.—Analysis of Variance

Source	d.f.	Mean Square	F
Between treatments	4	630·19	6·31*
Within treatments	94	99·93	
Total	98		

B.—Treatment Group Means Ranked in Order

C	P	ECT	D	D&P
37·47	38·75	41·55	48·75	49·65

NOTE: Any two means not underscored by the same line are significantly different (5 per cent. level test).
* $p<\cdot001$.

TABLE V

Source of Variance in MACC Ratings: Four Treatment Groups Only

Source	d.f.	Mean Square	F
Drugs	1	2420·62	24·16*
Psychotherapy ..	1	17·58	·18
Interaction ..	1	82·57	·82
Within treatments	75	100·2	
Total	78		

* $p<\cdot001$.

hospital one or more times. Altogether, 41 of the 100 patients were re-admitted at least once during the two-year period following their first release. For their first re-admission, 33 came back to Camarillo Hospital; one was re-hospitalized elsewhere in California, and seven others in other States or Mexico. Although there are apparent differences in re-admission rates (number of patients re-admitted) among the various treatment groups, these are not statistically significant when tested by the Chi square test ($p>\cdot70$).

4. *Length of Time in Hospital*

For potentially chronic disorders such as schizophrenia it is critical to determine how much of a patient's life is spent in hospital once he has been identified as schizophrenic. At present we are able to report the amount of time in hospital up to three years from the date of first admission to the study. Analysis of variance (Table VII) shows that the differences amongst the five groups would be declared significant at the 10 per cent. level but not at the 5 per cent. level. A New Multiple Range Test shows that the "control" and "psychotherapy" patients spent, on the whole, significantly more time in hospitals than the "electroshock" patients. The differences among other treatment groups were not statistically significant.

TABLE VI

Number of Patients Re-admitted within Two Years after First Release, by Treatment Group

	C	E	D	P	D&P
Number re-hospitalized	8	6	8	11	8
Number not re-hospitalized	12	14	12	9	12

$\chi^2=2\cdot18$, not significant, p ($>\cdot70$), d.f.=4.

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TABLE VII

Time in Hospital during Three Years Following First Admission

A.—Analysis of Variance

Source of Variation	d.f.	Mean Square	F
Between treatments	4	125448·66	2·40*
Within treatments	95	52281·72	
Total	99		

B.—Treatment Group Means (Days) Ranked in Order

ECT	D	D&P	C	P
214·4	276·05	299·3	374·4	395·4

NOTE: Any two means not underscored by the same line are significantly different (5 per cent. level test).
* $p < \cdot 10$.

DISCUSSION

In the present state of our knowledge, it seems highly unlikely that any one treatment for the syndromes known as schizophrenia will prove to be superior to all others in every respect and for every patient. It is, therefore, important to examine varied measures of outcome, to recognize the meanings and implications of each criterion used and, ultimately, to examine the question of treatment specificity—which treatment is likely to be best in what way for this particular type of patient? In the present analysis, there are issues on which evidence is relatively ample and clear-cut and others on which evidence and confirmation are still being sought.

It is reasonably evident that, by and large, patients treated with drugs, with or without psychotherapy, manifest healthier clinical pictures, as portrayed by the nurses' and psychoanalysts' ratings, than the control patients. Nurses' ratings also indicate that, in general, "drug" patients do better than those given "electroshock" or "psychotherapy alone", and there is a trend in the same direction in the psychoanalysts' ratings: the differences in this instance are less clear-cut, but they are consistent with differences previously reported in terms of other criteria (May (2); May and Tuma (3, 4)). It also appears that the effects of "drug" and "psychotherapy" do not interact significantly as measured by the nurses' and psychoanalysts' ratings.

The differences in re-admission rate did not reach an acceptable level of statistical significance, but it is worth noting that 19·5 per cent. of the re-admissions occurred in hospitals other than Camarillo, 17 per cent. outside California. This should warn the clinician to use great care in interpreting statistics from cohort studies based on data from one hospital only or from one single state.

It is often remarked that schizophrenia is a chronic disease and that recovery and return to the community is, at best, a temporary phenomenon. With this rather pessimistic view in mind and faced with an actual re-admission rate of 41 per cent. in three years, we asked the question: How much time will a schizophrenic patient spend in mental hospitals once he has been admitted for the first time? This is a fundamental question which requires a follow-up beyond the scope of the present study. What we can report, however, is the length of time spent in hospitals during a period of three years following first admission. Although the only statistically significant difference was between the electroshock group on the one hand and the

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psychotherapy and control groups on the other, the drug groups were close to the shorter end of the continuum. The difference between the "electroshock" and the other groups is of particular interest because this is the only criterion we have studied so far that favours electroshock over drugs. However, it would be well to be cautious in interpreting these findings on re-admission and overall hospital stay, particularly in the context of a relatively short period of follow up. Longer periods of follow up and the use of criteria relevant to a wider scope of post-hospital performance and level of adjustment are essential and will, we hope, be presented in future reports. We also expect to be able, at some time in the future, to report on the problem of which *type* of patient responds best or in what way to a particular type of treatment. If two treatment methods have equal improvement rates, this does not necessarily imply that they are effective for the same type of patient.

Summary

Forty-seven male and fifty-three female first admission schizophrenic patients in the middle section of the prognostic range were assigned by a random method to five treatment groups—"control" or basic care alone; "individual psychotherapy alone"; "tranquillizing drug alone"; "electroshock"; "individual psychotherapy plus tranquillizing drug". Treatment was given under close supervision under public mental hospital conditions, and multidisciplinary evaluation was carried out before and after treatment, with follow up for three years after first admission.

Patients treated with drugs, with or without psychotherapy, did significantly better than the control group, in terms of nurses' ratings on the MACC and psychoanalysts' ratings on the Menninger Health-Sickness Rating Scale. On both measures, "drug" patients did better than those given E.C.T. or psychotherapy, but this was statistically significant only for the MACC.

Patients given E.C.T. spent less time in hospital during the three years after first admission than those in the other groups, the difference being statistically significant for the comparison with the "control" and "psychotherapy" groups only. There were no significant differences in re-admission rates, nor was there any indication of significant interaction between the effects of drug and psychotherapy.

Since it is unlikely that any one treatment will be uniformly effective for all patients in every situation, it is important to use some discretion in the interpretation and application of these results. The writers hope to be able at some time in the future to report longer periods of follow up with criteria relevant to a wider scope of post-hospital performance and level of adjustment; and also to examine the problem of which type of patient responds best, or in what way, to a particular type of treatment.

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