FOR RELEASE
AM'S FRIDAY, FEB. 17

A PROPOSAL FOR THE TECHNICAL EVALUATION OF PSYCHIATRIC DRUGS

TESTIMONY BEFORE

HOUSE APPROPRIATIONS SUBCOMMITTEE ON LABOR-H. E. W. HEARINGS

ON FISCAL 1957 BUDGET (REP. JOHN FOGARTY, CHAIRMAN)

10:00 A.M., THURSDAY, FEBRUARY 16, 1956

by

DR. NATHAN KLINE - Orangeburg, New York

Director of Research, Rockland State Hospital, New York.

Mr. Chairman and members of the Committee:

Pharmaceuticals capable of modifying thought, behavior and feeling, may ultimately prove of equal or greater importance than the introduction of atomic power. In the history of civilization man has demonstrated his capacity to control virtually every aspect of the universe except himself. We are not yet near the point where pharmaceuticals will protect us from emotional infection and disease but the first steps have been made to show that subtle alterations of the chemical structure of the body can, in some cases, change violently assaultive psychotics to happy and productive individuals. This is not hearsay evidence: at Rockland State Hospital we have treated some three thousand patients and I have personally seen scores of these patients, once considered "hopeless", return to the community and take up their lives. As indicated in one of our recent publications, in one of our buildings for chronic patients less than 5% of the 740 residents were discharged in the year prior to the start of the new drug therapies. In the past year we have released 15%. Of the chronically ill so treated approximately 5% recover who would probably not have done so otherwise. In the more acute patients who have been ill a shorter length of time much higher percentages have been discharged. Attached is a table illustrating this point (Table 1). Even among

those not recovering sufficiently to be discharged some three quarters have shown some degree of improvement. Chronologically we are probably about where investigations of radioactive phenomena were at the turn of the century.

Since the last ice age most of mankind's major disasters have been self-incurred. The assaults against peace and progress were triggered by paranoid, guilt ridden, anxiety laden, depressed or otherwise emotionally disturbed deviants with delusions of grandeur or of world destruction. One can only conjecture what a future might be like in which there were not demagogues and dictators motivated by fear or hate or pathological ambition.

There were violent protests when anesthesia was introduced into surgery and childbirth on the grounds that man "was meant to suffer" but there are now very few who would choose to return to such barbarities as were then necessary. Many of the life-saving medical techniques would be impossible without anesthesia. The days of woman, at least, are no longer three score years and ten since by reason of the antibiotics and other medical advances the average life span is approaching 75 years. The Hoover Commission has pointed out, however, that there is little point in prolonging life "if we are to end ingloriously with the senile psychoses."

In my private practice I have had a number of business executives incapacitated by anxiety who were relieved by these medications. In a number of writers and artists long arid periods of non-productivity were "broken" with these treatments and in a sizeable number of housewives, lawyers, accountants and others, disabling fears and "psychosomatic" symptoms were sufficiently relieved to permit more effective psychotherapy.

Within the past two years many of the mental hospitals in the country have made a long step toward becoming treatment centers completely unlike anything known in the past. In a paper delivered before the Midwest Regional Research Conference of the American Psychiatric Association earlier this year, we estimated that five percent of the chronic schizophrenic patients in hospitals could be released if adequate applications of the pharmaceuticals then available were properly applied. The figures which

Dr. Brill, Assistant Commissioner of Mental Hygiene for the State of New York, will subsequently present seems strongly to confirm this estimate.

The millions of dollars of direct saving to the taxpayer is as nothing compared to the immeasurable saving in human suffering and social disruption which the illnesses of such individuals entail. The application of these drugs has undoubtedly spared many patients the need of being sent to a mental hospital. Knowing about the reported favorable results many patients are voluntarily seeking admission. The usefulness of these medications are illustrated not only by their widespread use but by the fact that the sale of barbiturates has been markedly reduced. Despite the fact that barbiturates in psychiatric patients act primarily to dull the senses or provide sleep which anxiety and worry prevent, there nevertheless has been manufactured about 600,000 lbs. per year in the United States. When one takes into account one pound provides approximately 5,000 doses of medication, the sale of 3,000 tons of this material means a total of 3 billion doses. By the reports of two manufacturers of barbiturate the sale in 1954 dropped to about 82% or 83% of the 1953 figure and in 1955 the sale had dropped to below 60% of the 1953 base line. Both companies attributed this drop to the substitution of more effective medications -- primarily reserpine and chlorpromazine.

Newer preparations are now being tested and as the drugs become safer and more effective new and different applications become possible. An editor of one of this Nation's best known publications suffered acutely in the high pressure conferences to which his work subjected him. Not only was his efficiency reduced but his overreaction to his colleagues in turn reduced the effectiveness of some of the meetings. He now finds that by taking a suitable amount of medication an hour or two before his conferences that he no longer becomes upset and is able to function much more effectively. But we hasten to add that other private patients in similar situations do not always respond with uniform success. We are still fumbling at the beginning of knowledge and what we do not know is much greater than what we do know.

Let me emphasize that although the pharmaceuticals presently available sometimes and in some cases do bring about improvement that our ignorance of the proper

applications of these medications, of how they work, and of what new ones may eventually be produced is still minute compared to what must yet be done. Our appearance before this committee today is not only to bring to your awareness the hopeful developments in the field of mental health and mental disease. The Congress is in a position to perform both an important and a necessary function by making it possible to implement a nation-wide study of how and where the drugs presently available can most effectively be applied, and also to provide a stimulus for research into new pharmaceuticals and new methods of applications. Since I had the good fortune to introduce one of these groups of drugs -- the Rauwolfia alkaloids, including reserpine, into the treatment of psychiatric patients (so far as our Western civilization is concerned) I have been consulted by any number of individuals and groups of individuals who saw a potential usefulness for such drugs. Projects involving the treatment of drug addicts, of juvenile delinquents, of alcoholics and a host of other of our social problems have all shown promise. Our one great lack has been a definitive study on a nation-wide basis and it is on this particular aspect of the problem that I would like to propose that action should be taken.

On the attached sheet, with the help of Dr. Brill, I have outlined a project which would fulfill this need. In a hospital such as Rockland State we have seen graphically and dramatically what the drugs are capable of doing. In the attached figures (Figs. 1, 2, 3) it is obvious that restraint, seclusions and camisoles have been markedly reduced since the introductions of these new treatments. Since treatment with the new drugs has been vigorously applied the disturbed wards are now quiet, patients are no longer in restraints or camisoles, there are curtains at the window, vases of flowers on the tables and recently when I was showing a visitor through, patients were cutting out and sewing costumes for a ward party. Two years ago to have brought a pair of scissors or any sharp instrument on the ward would have been not only unwise but dangerous. Now they are something that is of therapeutic help to the patient. We know that the calming effects of the drug are almost universal wherever and whenever applied. The degree of effectiveness in getting patients well

enough to not only leave the hospitals but to remain useful members of the community is something much more in dispute. It is particularly in this respect that the nation-wide evaluation under a variety of settings is necessary to determine to whom and how the drug should be used. The Congress has a history of having most effectively implemented similar projects in respect to streptomycin and cortisone. In this area of even greater economic and social importance it would therefore seem most appropriate to request that a similar project be supported.

There is strong evidence that the excited disturbed patients do somewhat better than the quiet ones and we know quite definitely that the shorter time a patient has been hospitalized the better are his chances of discharge. We would propose that both disturbed and non-disturbed (both acute and chronic) patients be investigated in five different hospitals at various points throughout the country. For reasons explained in the attached sheet we feel that only adults should be included in the present project and they should be limited to schizophrenic psychoses and be between the ages of 20 and 45 years. The patient should be free of organic disorders and since the facilities in the community are better for return of such patients, we believe they should be female. It is estimated that six months will be required to assemble suitable personnel and that another three months will be consumed in selecting the patients -- eight hundred in all, who would be included in the investigation. Six months would be a minimum period for treatment following which another three months would be needed to evaluate the degree of improvement achieved. The acute and immediate use of the drugs could then be estimated allowing an additional half year for statistical analysis and preparation of report. This phase of the project would therefore occupy two years. There remains, however, a continuing problem since it is of at least equal importance to know whether the patients improving by means of these treatments are able to remain out of the hospitals. It is, therefore, recommended that half of the patients be continued on medication at the end of the six months treatment period and the other half either be discontinued or placed on tablets which are identical with the original active preparations except that they contain none of the active drug. The patient should be evaluated

yearly (particularly those who are discharged from the hospital) to determine the long term action of such preparations.

At the present time there appear to be only two drugs which have been widely enough tested to justify inclusion under this project. These are reserpine (previously referred to) and chlorpromazine which appears to produce an equal degree of improvement - but not always in the same type of patient. The use of these two drugs in combination would constitute a third method of treatment which it is necessary to test and a fourth group of patients should be included in the above design to receive identical tablets which are pharmacologically and chemically known not to produce the same effects. This last group, since they will not be receiving the therapeutic action of the drugs, will act as a control to determine whether it is merely the administration of any kind of a pill or the drugs themselves which are effective in making possible the release of patients from the hospital. The acute patients in this group should receive the best psychotherapy available (at least 3 times a week) so that they will be actively treated but by a different method. In the project outlined the funds requested are not so much for the purchase of the drugs but for the employment of the highly skilled personnel necessary to carry out such a piece of investigation.

In addition to the million dollars requested for the overall nation-wide evaluation it would be equally important that a like amount be set aside for the investigation of new drugs and new applications of the drugs already available. Many of my colleagues are working at such projects but all of us are hampered to some degree by inadequate funds for the careful evaluation of the effects of such medications.

Investment of money for this purpose is not only an investment in the present since there will be immediate practical returns, but it is also making possible future developments of probably even greater significance.

PRESENTED AT THE AMERICAN ACADEMY OF PSYCHOSOMATIC MEDICINE MEETING 1955

TABLE I

IMPROVEMENT OF DRUG TREATED PATIENTS
RELATIVE TO DURATION OF HOSPITALIZATION

Duration	Marked	Moderate	Slight	None	No. of Cases
less than 1 year	64%	16%	13%	6%	67
1 to 3 years	33%	25%	26%	16%	141
3 to 5 years	25%	30%	30%	16%	126
more than 5 years	6 1/2%	31%	44%	19%	366

Relapse rate of approximately 1/3 from these figures

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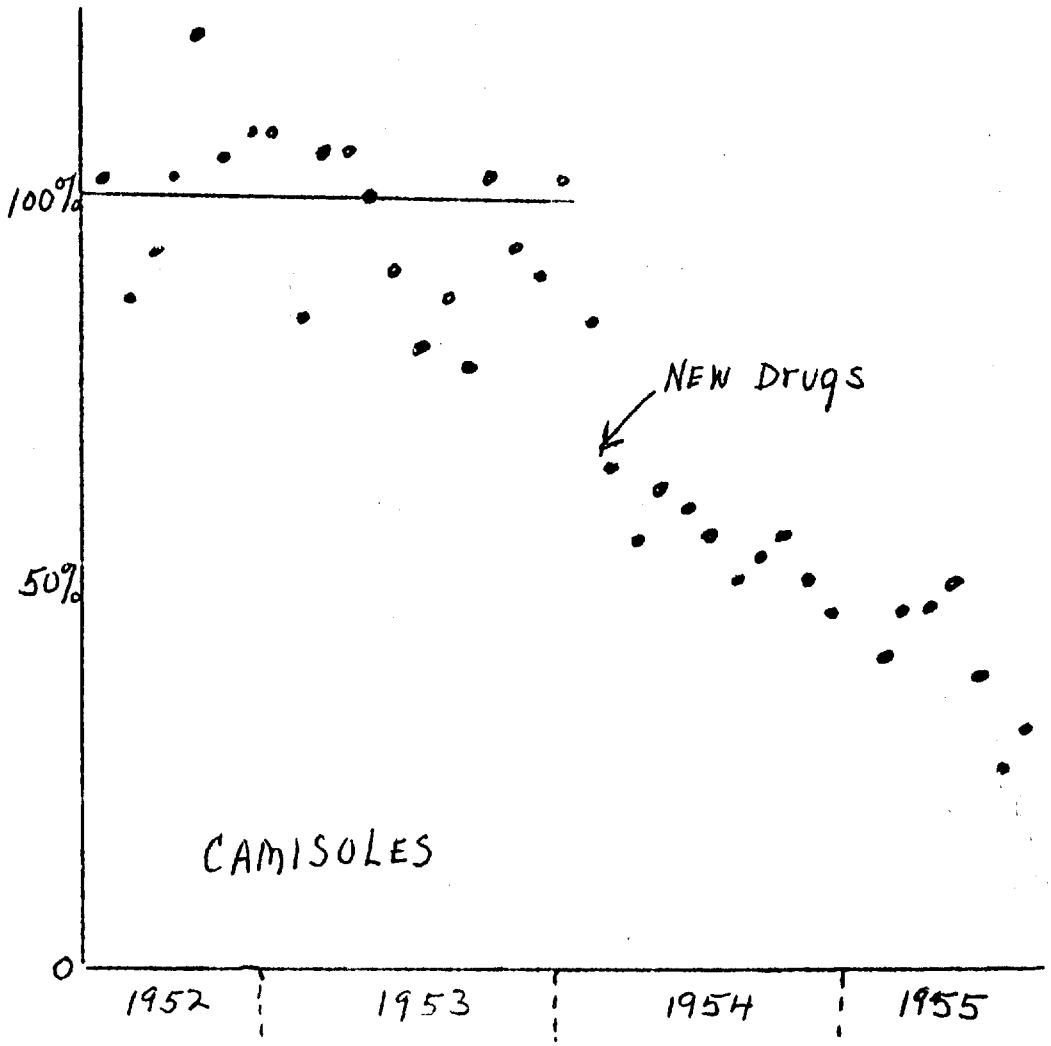

FIG. I

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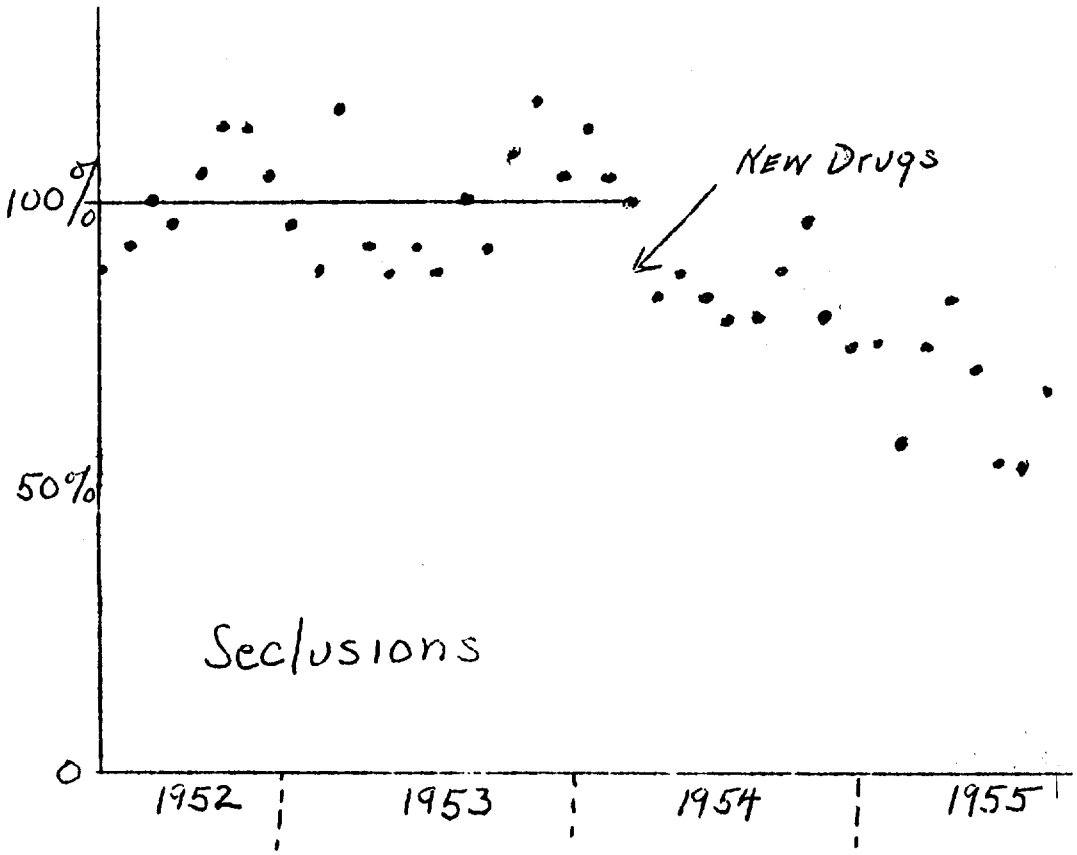

FIG. 2

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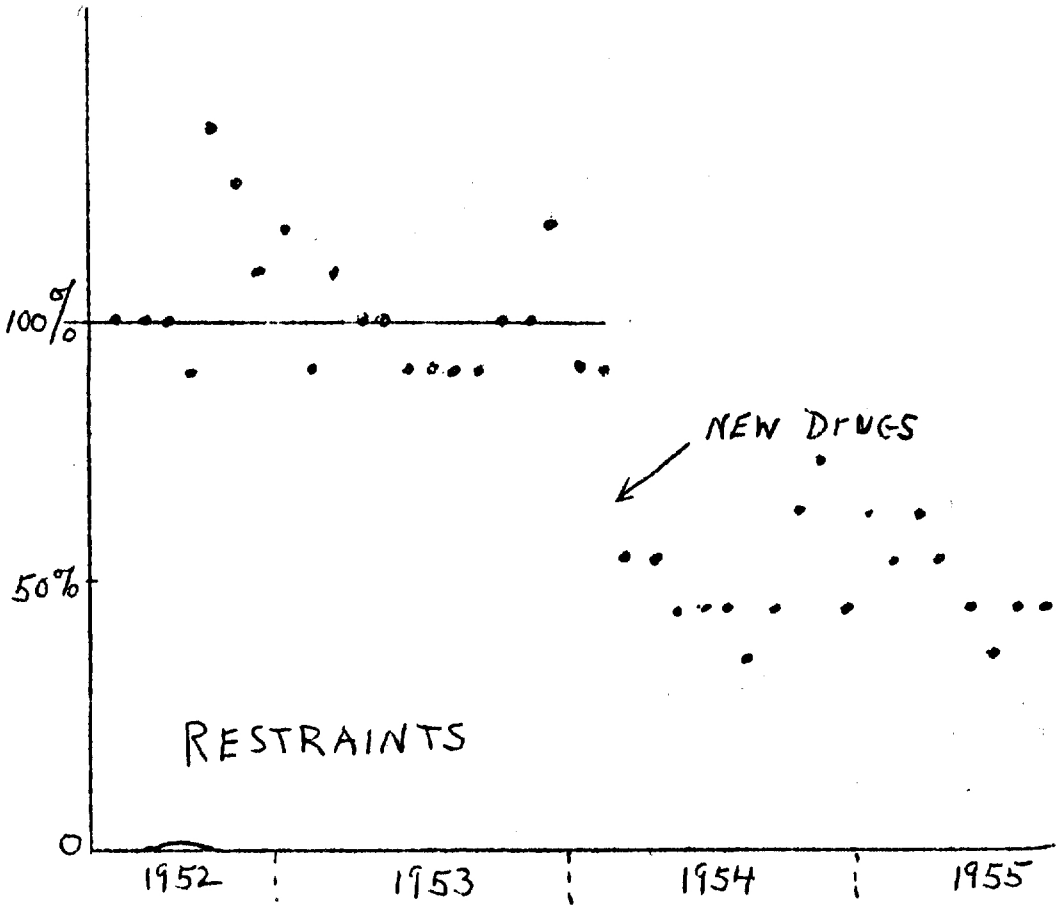


FIG. 3

APPENDIX A

A PLAN AND A DETAILED BUDGET FOR AN EVALUATION OF THE NEW DRUGS

The table of organization would be as indicated in the scheme below. The National Institute of Mental Health would appoint a director for the project whose responsibility would be to see to the implementation of the proposal. It would be necessary for him to have secretarial assistance and the use of a chief statistician with suitable statistical assistance in setting up the project.

The director would select five hospitals encompassing a variety of social and economic milieus. Ratings such as those provided in the NIMH report on psychosurgery (edited by W. Overholser) might provide such a basis with one hospital being drawn from each twenty percentile. It would be necessary that the hospitals be those in which the drugs had not yet been extensively used or where doses had been so low that to all effects and purposes they had not been tried at therapeutic levels. It would also be necessary that the records be adequate for clinical purposes. The director would be responsible for contacting the appropriate state authorities and obtaining their consent and cooperation in the project. At each of these hospitals, a non-physician administrative assistant to the Director should be appointed from the regular hospital staff and for the duration of the investigation be paid by the project. He should be thoroughly familiar with the hospital's record-keeping system and it would be his responsibility to undertake the preliminary screening of the records and provide the list of patients who might be suitable for investigation. There also should be appointed at the hospital a liaison medical officer who would be supported by the project, who would review each of the patients to determine whether their current status is such that they actually do meet the criteria. The criteria for inclusion are tentatively suggested as follows:

1. Females -- to make the group as homogeneous as possible. 2. Certified patients -- this would reduce the likelihood of patients withdrawing from the project after it has been started. 3. Functional psychoses -- these should be as nearly classical cases of schizophrenic psychoses as can be obtained. 4. Age range should be from twenty to forty-five years -- this will help avoid the problem of adolescence or changes which occur with aging. 5. Free of organic disorders -- this would eliminate the likelihood that the disease might be due to changes other than the basic psychiatric disorder. 6. First admissions -- it is obviously difficult to estimate the duration of illness before admission but in the acute cases particularly, care should be taken to make certain that these are not patients who have been ill for a long time and merely maintained at home.

Although in the final project there should be forty patients of the chronic disturbed type, forty patients of the chronic non-disturbed type, forty of the acute disturbed and forty of the acute non-disturbed in the preliminary screening at least an additional fifty percent in each group should be provided so that replacements are available if a patient must be discontinued for any reason whatsoever.

It is recommended that each group of forty patients be placed on one ward so that there is continuity of similar environment and personnel. This would require four separate wards and it is recommended that in order to have careful records that the project provide to the hospital four nurses for each of the wards so that one of them may be on duty at all times. In addition, a secretary would be necessary for maintenance of records and a lab technician with necessary equipment to keep check on possible side effects which require laboratory testing.

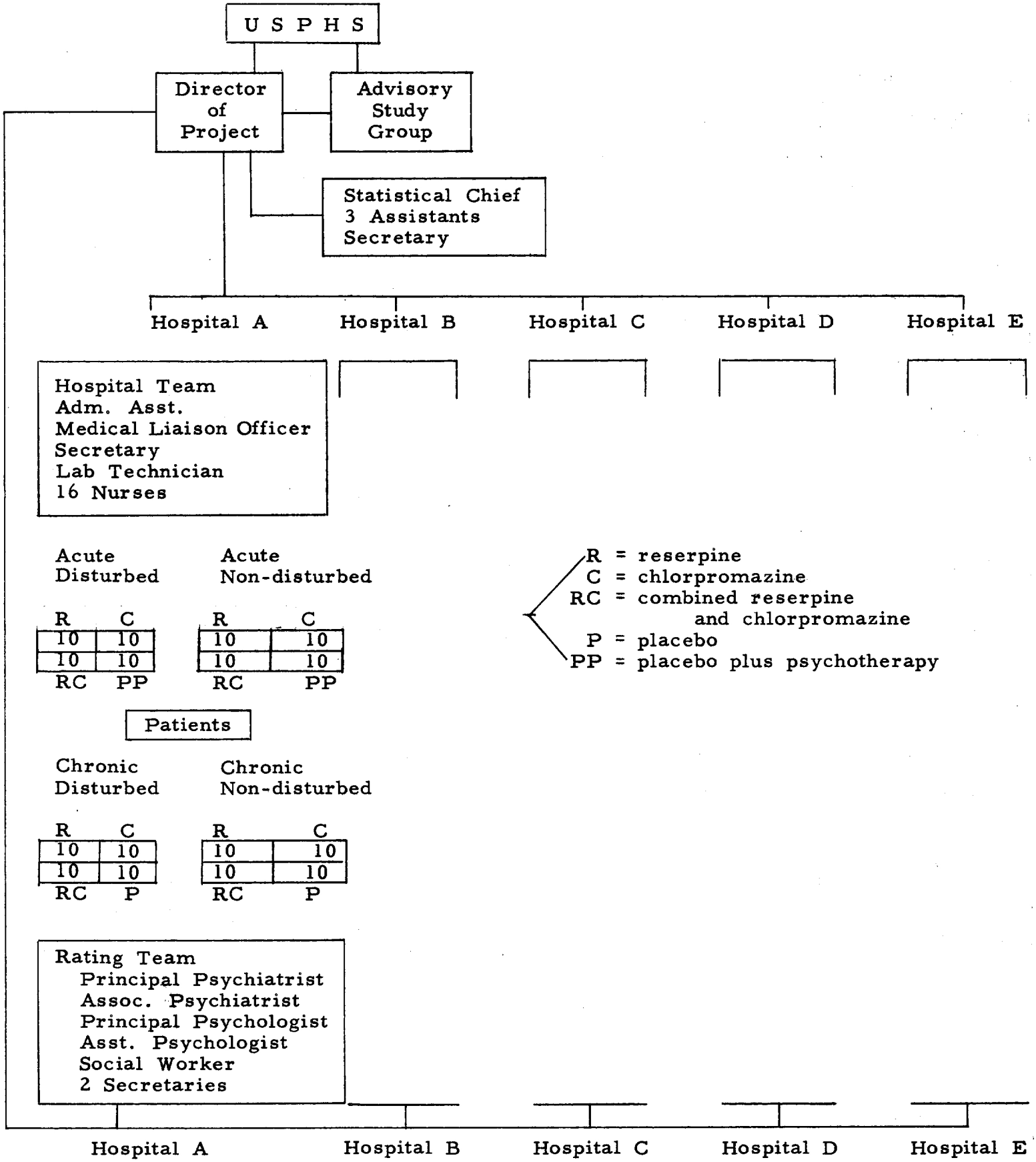
Once the basic patient group has been selected along with the fifty percent replacement reservoir, a rating team composed of a principal psychiatrist with an associate psychiatrist, a psychologist with an assistant and a social worker should be brought in from outside the hospital. It is recommended that they be drawn from the Department of Psychiatry at a nearby University Medical School but preferably one not ordinarily servicing the hospital in any way. The function of the group is to evaluate the psychiatric and psychological status of each patient. The emphasis should be placed on the social worker to ascertain as far as possible that patients taken into the project would have places in the community if their improvement were sufficient to warrant it.

After evaluation of the patients in respect to their current status and probable prognosis, the patients should be treated for a period of six months with adequate doses of the drugs. In the case of the acute patients it is felt necessary for patients not receiving active drugs to be given intensive psychotherapy (a minimum of three hours per week for the period during which other patients are placed on active drugs). It is believed valuable to give these patients identical pharmaceuticals except that they would be non-active. The patients placed on drug therapy should be handled in the ordinary hospital manner and not given the benefit of additional psychotherapy. The choice of psychotherapist would rest with the Director of the project and the Superintendent of the hospital or the Commissioner of Mental Hygiene of the State.

No patient should be considered a failure unless he has been treated for three months with a minimum of four hundred milligrams of chlorpromazine daily until the patients had improved sufficiently to be considered for discharge or until the end of the project treatment phase. With reserpine three milligrams orally

and five to ten milligrams intramuscularly for at least the first six weeks and a maintenance dose of three milligrams until discharge or until improvement was such that it was felt medically advisable to reduce the dosage. On combined reserpine-chlorpromazine treatment two milligrams orally and fifty to one hundred milligrams chlorpromazine would be considered minimal dosage unless there were strong medical indications otherwise. At the end of the six months treatment period the group would again be evaluated by the original rating team. Those patients who had improved sufficiently to have left the hospital should be recalled for the time during which the ratings occurred. Treatment should be continued during the evaluation period as medically indicated.

Another six months would be required to statistically analyze and prepare a report on this project. This would provide definitive information on the use of the drugs in the intensive phase of treatment. It is believed that half of the patients able to leave the hospital should be continued on maintenance doses of the drugs they are receiving whereas the other half should be discontinued. Selection should be on a random basis. In the event of relapse patient should be retreated and discharged on maintenance dose if improvement occurs a second time. It is suggested that the forty patients in each of these sub-groups be first selected and then randomized into the four sub-groups in order to avoid any systematic bias. In the same manner five of each of the ten patients in each cell should be randomly selected before the project begins to determine which of them will be continued on maintenance doses subsequently. Replacements, as indicated above, should be available.


U S P H S
Director of Project
Advisory Study Group
Statistical Chief
3 Assistants
Secretary
Hospital A
Hospital B
Hospital C
Hospital D
Hospital E
Hospital Team
Adm. Asst.
Medical Liaison Officer
Secretary
Lab Technician
16 Nurses
Acute Disturbed
R C
10 10
10 10
RC PP
Acute Non-disturbed
R C
10 10
10 10
RC PP
R = reserpine
C = chlorpromazine
RC = combined reserpine and chlorpromazine
P = placebo
PP = placebo plus psychotherapy
Patients
Chronic Disturbed
R C
10 10
10 10
RC P
Chronic Non-disturbed
R C
10 10
10 10
RC P
Rating Team
Principal Psychiatrist
Assoc. Psychiatrist
Principal Psychologist
Asst. Psychologist
Social Worker
2 Secretaries
Hospital A
Hospital B
Hospital C
Hospital D
Hospital E

BUDGET

Personnel

Central Office				
Director -	$22,000			
Advisory Study Group	3,000			
Statistical Chief	12,000			
3 Asst. Statisticians @ $4,500 --	13,500			
Secretary	3,500		54,000	
Hospital Teams				
Adm. Ass't.	5,000			
Medical Liaison Officer	10,000			
Secretary	3,500			
Lab Technician	4,000			
16 Nurses @ $4,500 --	72,000			
	94,500	x 5 =	472,500	
Rating Teams				
Principal Psychiatrist	15,000			
Assoc. Psychiatrist	10,000			
Principal Psychologist	12,000			
Asst. Psychologist	8,000			
Social Worker	10,000			
2 Secretaries @ $3,500	7,000			
	62,000	x 5 =	310,000	836,500

Equipment

Laboratory Equip. for technician	3,000 x 5 =	15,000	
Calculators for statisticians	500 x 3 =	1,500	
Office furniture for central office (Director Chief Statistician, etc.)		3,000	
Office furniture for rating teams and hospital teams	2,500 x 10 =	25,000	
Filing cabinets, typewriters, etc. for central office, rating teams, hospital		3,500	48,000

BUDGET - Continued

Rent			
Central Office		3,000	
Car for Social Worker	$1,000 x 5 =	5,000	8,000
Supplies			
Laboratory	500 x 5 =	2,500	
Office (Central, Rating and Hospital)		6,500	
Medications (Reserpine and Chlorpromazine)		40,000	49,000
Travel			
Advisory Study Group, Director, Rating Teams, etc.			25,000
Miscellaneous			
Cleaning woman, overhead at hosp. etc.			33,500
			$1,000,000