Predicting the Relief of Anxiety With Meprobamate

Nondrug Factors in the Response of Psychoneurotic Outpatients

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AS THE minor tranquilizers gain increasing acceptance in the treatment of ambulatory psychiatric patients, a closer delineation of their clinical effects and the most favorable circumstances for their use become important considerations. This report is one of a series based on a multiclinic, placebo-controlled trial of meprobamate in anxious outpatients, directed toward these questions.[1]

Method

The study was designed originally to determine whether the doctor's expressed attitude toward the prescribed medication influences the effect of the drug (defined as the difference in response to drug and placebo). Psychoneurotic outpatients, 138, manifesting anxiety were treated for six weeks with medication and brief, supportive interviews every two weeks with a psychiatric resident. The patients were divided among 12 ($2 \times 2 \times 3$) different treatment conditions composed of: (1) meprobamate 400 mg, q.i.d., vs an identical placebo in a double-blind arrangement; (2) a doctor expressing an enthusiastic attitude toward the medication vs a doctor expressing a skeptical attitude toward the medication; and (3) three different psychiatric outpatient clinics.

The patient reported his symptomatic condition before each interview by means of five ratings. These ratings included an overall 7-point judgment of change, a checklist of 64 common symptoms, a score based on the patient's presenting (target) complaints, and an adjective checklist for registering anxiety and depression. The patient rated each complaint or adjective on a 4-point scale, and totals were computed by adding the scores for individual symptoms.

Early Results

The original analyses showed differential treatment effects mainly in the overall judg-

Table 1.—*Anxiety Symptoms*

Nervousness or shakiness inside

Faintness or dizziness

Sweating

Trembling

Suddenly scared for no reason

Feeling fearful

Heart pounding or racing

Trouble getting your breath

Hot or cold spells

A lump in your throat

Feeling tense or keyed up

ments of change and the patient's score for presenting complaints on the symptom checklist. The results at one clinic showed the expected interaction between medication and doctor's expressed attitude: with the enthusiastic doctors, patients taking meprobamate improved more than patients taking placebo; whereas with the skeptical doctors, patients taking placebo tended to improve more than patients taking meprobamate. At the other two clinics, however, this interaction was absent or possibly reversed, with meprobamate tending to be superior to placebo with the skeptical doctors.

In order to determine the more specific effects of the treatment conditions, further analyses were done in terms of the scores for six symptom clusters (anxiety, depression,

Table 2.—*Characteristics of 107 Patients and Their Treatment*

Characteristic	N	Range	Mean	SD
Clinic				
Johns Hopkins Hospital	42			
Pennsylvania General Hosp	32			
Univ of Pennsylvania Hosp	33			
Medication				
Meprobamate	53			
Placebo	54			
Previous outpatient admission				
Yes	34			
No	73			
Duration of illness				
Up to 6 mo	28			
Over 6 mo	79			
Previously treated with psychotropic drugs				
Yes	83			
No	24			
Patient's treatment goal				
Psychological readjustment	23			
Relief of psychological symptoms	41			
Relief of physical symptoms	29			
Other	14			
Age, yr		13-59	32.93	8.55
Sex				
Male	38			
Female	69			
Race				
White	44			
Negro	63			
Marital status				
Single	31			
Married & widowed	56			
Separated & divorced	20			
Educational levels (6 levels)		1-6	4.11	1.03
Employed now				
Yes	39			

anger-hostility, obsessive-compulsive, phobic, and unclassified) developed on the basis of clinical judgment and five factors (neurotic feelings, somatization, performance difficulty, depression, and fear-anxiety) derived empirically from the patients' symptom checklist reports.[2] This procedure provided a much simpler and more direct picture suggesting that meprobamate administered for six weeks has an important, specific effect in reducing anxiety and somatic symptoms.

Method for Predictor Analysis

This paper reports more recent analyses of the change in anxiety level among the patients in the study described above, in relation to the medication they received and 29 other charac-

teristics of the patient and the treatment situation, particularly the patient's treating doctor.

The present analyses were performed by means of a multiple covariance procedure programmed for the IBM 7094.[3] This procedure provides estimates of the independent, simultaneous effects of several variables, including both quantitative data, such as age, and qualitative (classification) data, such as marital status. It also allows for a disproportionate distribution of subjects among categories in classification data. The procedure offers the option of searching stepwise a set or pool of independent variables for the subset which best describes the change in the dependent variable. This option selects only the most important of several highly correlated variables. The method combines in effect the functions of analysis of variance, analysis of covariance, and multiple

Table 2.—*Characteristics of 107 Patients and Their Treatment (continued)*

Characteristic	N	Range	Mean	SD
Employed now				
No	41			
Housewife	27			
Off drugs during past week				
Yes	75			
No	32			
Patient's attitude toward drugs (very eager to somewhat reluctant)		1-4	2.65	0.82
Prognosis				
Good	11			
Fair	74			
Poor or uncertain	22			
Weight in lb		100-256	143.65	29.26
Symptom distress scores				
Anxiety		1-28	11.78	6.20
Depression		0-28	9.32	5.72
Anger		0-11	3.22	2.42
Compulsive		0-10	3.00	2.61
Phobic		0-3	0.89	1.07
Unclassified		3-75	27.20	15.83
Doctor's role				
"Therapeutic"	56			
"Experimental"	51			
Doctor's comfort with patient (extremely comfortable to generally uncomfortable)		1-3	1.72	0.66
Doctor likes patient (much less than most to much more than most)		1-5	3.06	1.05
Doctor's drug attitude (Mason-Sachs Scale)		−14-8	−1.55	6.22
Doctor's F-scale score		11-46	27.33	10.58
Doctor's A-B scale score (A is high)		−3-3	0.33	1.75
Doctor's year of residency				
1	59			
2 or 3	48			
Doctor's social class index (family of origin, Hollingshead)		11-49	27.90	14.13

Table 3.—Analysis of Variance and Regression for Characteristics Selected From Pool

Characteristic					Regressor				
No.	Name	df	MS	F	No.	b	SE	t	Mean
5	Initial anxiety symptom score	1	350.69	28.06	6	0.46	0.09	5.30	11.78
10	Initial unclassified symptom score	1	57.63	4.61	11	−0.07	0.03	2.15	27.20
18	Race	1	92.99	7.44	21	−2.13	0.78	2.73	0.41
15	Treatment goal	3	36.57	2.93	16	−1.00	1.30	0.77	0.22
					17	0.97	1.15	0.85	0.38
					18	−1.57	1.22	1.29	0.27
3	Medication	1	4.76		4	1.05	1.71		0.50
19	Marital status	2	18.60		22	1.29	1.66		0.29
					23	−0.66	1.52		0.52
49	Marital status x medication	2	64.34	5.15	58	−1.69	2.17	0.78	0.13
					59	3.57	2.00	1.78	0.24
26	Weight	1	123.29		32	−0.05	0.02		143.65
56	Weight x medication	1	95.49	7.64	68	0.07	0.03	2.76	−0.51
25	Doctor's liking of patient	1	42.04		31	0.91	0.50		3.06
55	Doctor's liking of patient x med	1	100.41	8.04	67	−2.06	0.73	2.83	−0.01
27	Doctor's drug attitude	1	26.75		33	−0.11	0.08		−1.55
57	Doctor's drug attitude x med	1	58.00	4.64	69	0.28	0.13	2.15	0.30
	Total regression	17	81.14	6.49					
	Error	89	12.50						
	Total	106	23.51						
	Correction term	1	764.45			3.31			2.67

$R^2 = (17 \times 81.14)/(106 \times 23.51) = 0.55$

Table 4.—Unclassified Symptoms

Headaches
Being unable to get rid of bad thoughts or ideas
Bad dreams
Difficulty in speaking when you are excited
Trouble remembering things
Pains in the heart or chest
Itching
Feeling confused
Feeling shy or uneasy with the opposite sex
A feeling of being trapped or caught
Twitching of the face or body
Pains in the lower part of your back
Feeling blocked or stymied in getting things done
Worrying or stewing about things
Sex dreams
Unsatisfied with sexual partner
Your feelings being easily hurt
Having to ask others what you should do
Feeling others do not understand you or are
   unsympathetic
Feeling that people are unfriendly or dislike you
Nausea or upset stomach
Feeling inferior to others
Soreness of your muscles
Loose bowel movements
Difficulty in falling asleep or staying asleep
Difficulty making decisions
Wanting to be alone
Your mind going blank
Numbness or tingling in parts of your body
Trouble concentrating
Weakness in parts of your body
Feeling others are too critical of you
Heavy feelings in your arms or legs

regression analysis in a form sufficiently flexible to cope with many problems in the statistical evaluation of quantitative observations in real life situations.

The criterion in the present analyses was the change in the patient's report of distress on the cluster of anxiety symptoms across the six weeks of treatment in the study. The symptoms composing the cluster were selected from the 64 symptoms on the checklist by consensus of at least 15 out of 20 psychiatrists. The 11 items in the cluster are listed in Table 1.

Table 2 lists the 30 characteristics of the patient and the treatment situation that figure in the present analyses (note that each initial symptom cluster score counts as one characteristic). The values shown in the table are for 107 of the original 138 patients, who had complete data on all 30 characteristics and who actually entered into the new analyses. Since the procedure converts each classification into dummy variables numbering one less than the number of categories, the 30 characteristics were represented in the analyses by 36 independent variables.

In order to evaluate the effect of each characteristic upon the patients' *differential* responses to drug and placebo, 35 additional independent variables to assess the statistical interaction between medication and each other characteristic were included in the analyses. These additional variables to assess interactions of incidental interest brought the number of independent

variables or regressors in the analyses to a total of 74.

Two analyses were performed. The first was a multiple covariance analysis of the anxiety change scores in relation to the complete set of 74 independent variables without the search option. This nonsearch analysis resembled the usual multiple regression analysis. During inversion of the correlation matrix, the procedure dropped from the analysis 11 characteristics represented by variables highly correlated ($R > 0.95$) with the preceding variables in the matrix. This deletion feature was incorporated in the computer program on grounds that highly correlated variables: (1) might reduce the accuracy of computation during matrix inversion and (2) would not add appreciable information to the result.

In the second analysis, the 74 independent variables in the set or pool were searched stepwise for the subset contributing most reliably to the change in the anxiety symptom cluster score. To be selected by the search analysis from the pool and to remain in the selected subset, the variable(s) representing a characteristic was required at every step to show an F-ratio of at least 2.76 (for 1 df). This value represented approximately the 10% level of significance in the present case with 107 patients.

Results of Predictor Analysis

The nonsearch multiple covariance analysis revealed a multiple correlation of $R = 0.86$ between the change in anxiety score and the complete pool of independent variables. The full set of variables, then, accounted for about $R^2 = 74\%$ of the variation in the criterion. The overall F-ratio was 2.301, with a computed $P = 0.002$. These results indicated that the variables in the pool made an important contribution to the observed change in the patients' anxiety level across the six weeks of treatment in the study.

The stepwise search analysis of the pool of independent variables revealed a relatively small subset which jointly contributed most to the relief of anxiety. Table 3 shows the multiple covariance analysis which emerged from the search procedure. The variables in the table gave a multiple correlation of $R =$

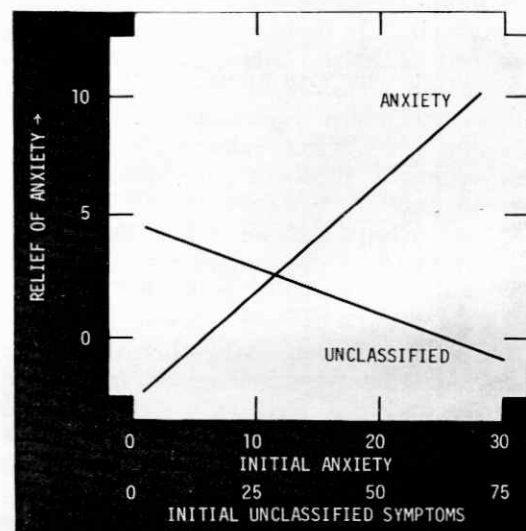**Table 5.—Predictors of Relief of Anxiety Selected by Search Procedure**

Predictor	Relief Predicted With	
	Placebo	Meprobamate
Higher initial anxiety symptom score	More	More
Lower initial unclassified symptom score	More	More
Negro race (vs white)	More	More
Seeks relief of psychological symptoms or other goals (vs relief of physical symptoms or adjustment)	More	More
Married or widowed (vs single, separated or divorced)	Less	More
Greater body weight	Less	More
Doctor likes patient less	Less	More
Doctor more favorable toward drugs	Less	More

0.74 with the criterion, explaining about $R^2 = 55\%$ of its variation.

The search procedure selected two types of variables related to change in anxiety. One type "predicted" relief without respect to medication (main effects). All the variables of this type represented characteristics of the patient. Another type "predicted" different degrees of relief for patients treated with meprobamate and for patients treated with placebo (interaction effects). Some variables of this type represented characteristics of the patient and some represented characteristics of the treating doctor.

Patient Characteristics That Predicted Relief Without Respect to Medication

Fig 1.—Relief of anxiety symptoms in relation to initial level of anxiety symptoms and initial level of unclassified symptoms.
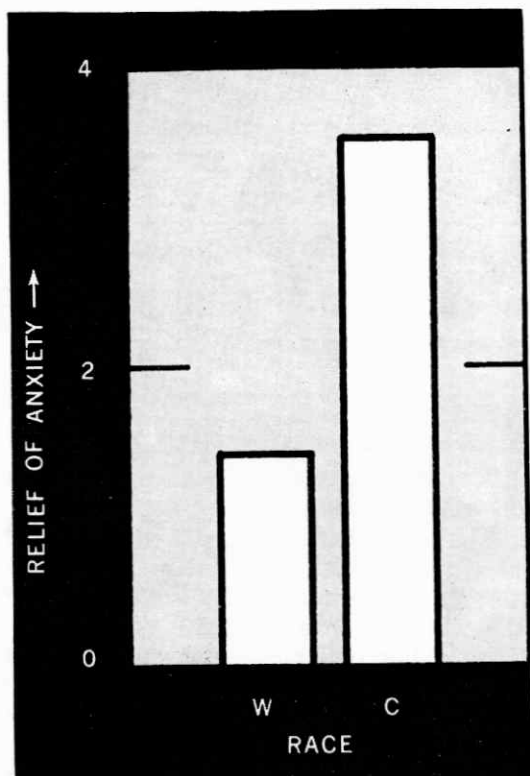
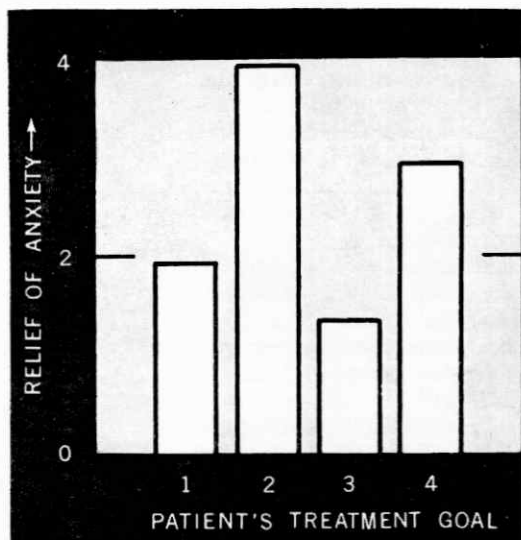Fig 2.—Relief of anxiety symptoms in relation to race.

Fig 3.—Relief of anxiety symptoms in relation to patient's treatment goal: 1, psychological readjustment; 2, relief of psychological symptoms; 3, relief of somatic symptoms; and 4, other goals.
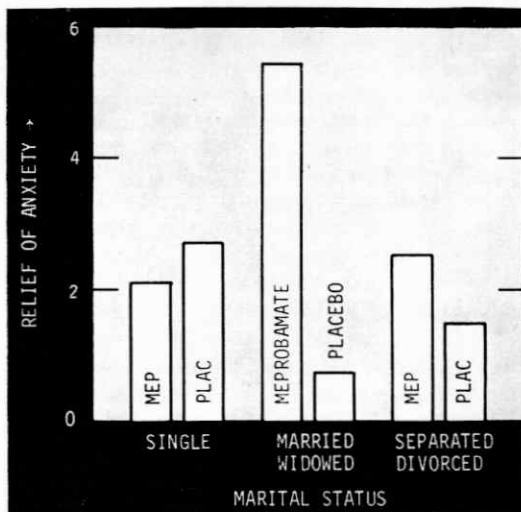

Fig 4.—Relief of anxiety symptoms in relation to type of medication and marital status.

(*Main Effects*).—Two aspects of the patient's presenting symptom picture were related to relief of anxiety, as shown in Fig 1. Patients with higher initial levels of anxiety experienced more relief. Patients with higher initial scores on a cluster of unclassified symptoms from the checklist, however, experienced less relief. Table 4 lists the unclassified symptoms. More than one third of these symptoms represent somatic complaints, and the remainder represent mainly interpersonal problems and difficulties in performance.

The patient's race was related to relief as shown in Fig 2. Negro patients experienced more relief than white patients.

The patient's treatment goal as judged by the psychiatric consultant after the initial evaluation interview, was related to relief as shown in Fig 3. Patients seeking relief of psychological symptoms experienced most relief, and patients seeking relief of physical symptoms experienced least relief. Patients seeking psychological readjustment or other objectives experienced intermediate degrees of relief.

Patient Characteristics That Predicted Different Degrees of Relief With Meprobamate and Placebo (Interaction Effects).—The patient's marital status and medication were related to relief as shown in Fig 4. Married and widowed patients responded relatively more to meprobamate than did single, separated, or divorced patients.
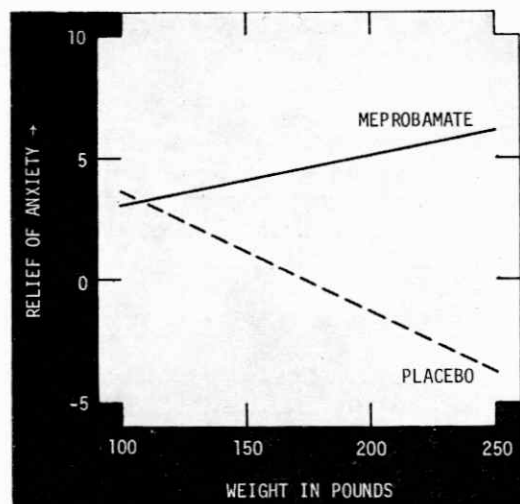
Fig 5.—Relief of anxiety symptoms in relation to type of medication and body weight.

Fig 7.—Relief of anxiety symptoms in relation to type of medication and doctor's attitude toward drug therapy.
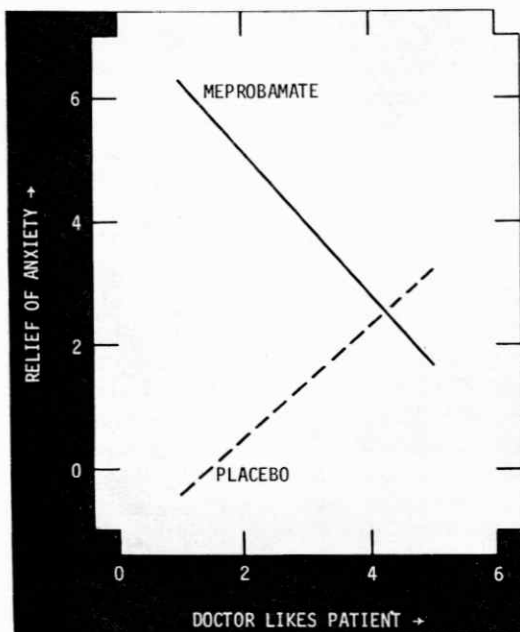

Fig 6.—Relief of anxiety symptoms in relation to type of medication and doctor's liking of patient.

The patient's weight and medication were related to relief as shown in Fig 5. Heavier patients responded relatively more to meprobamate than did lighter patients.

Characteristics of the Treating Doctor That Predicted Different Degrees of Relief With Meprobamate and Placebo (Interaction Effects).—The doctor's liki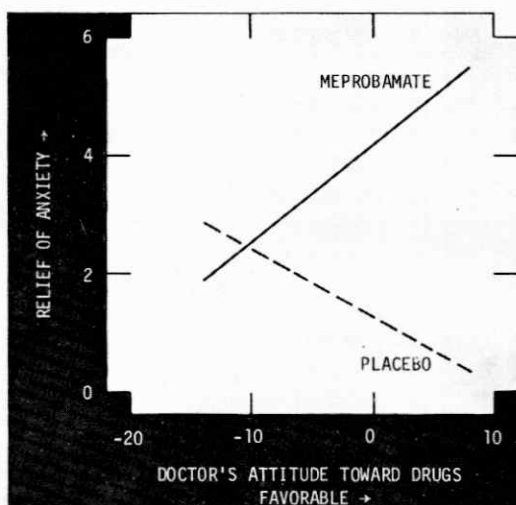ng of the patient and medication were related to relief as shown in Fig 6. Patients who were liked less by their doctor responded relatively more to meprobamate than patients who were liked better.

The doctor's attitude toward drug therapy, as measured by a scale devised by Mason and Sacks,[4] and medication were related to relief as shown in Fig 7. Patients treated by a doctor with a more favorable attitude toward drug therapy responded relatively more to meprobamate than did patients treated by a doctor with a less favorable attitude toward drug therapy.

The findings presented above are summarized in Table 5.

Comment

In terms of accounting for the variation in the criterion, the more comprehensive new analyses presented above compare favorably with the original analysis which related the change in anxiety score only to initial anxiety level and the main treatment effects: medication, doctor's expressed attitude toward medication, and clinic. These variables and their interactions gave a multiple correlation of $R = 0.60$ with the criterion, explaining about $R^2 = 36\%$ of its variation. The error mean square in the original analysis was about 50% greater than the error mean square in the new analyses. Evidently a noteworthy gain in predictive power was achieved by including the additional charac-

Table 6.—Correlations Between Predictors Selected From Pool and Variables Remaining in Pool

Predictors Selected	Correlated Variables	Pearson's r
Medication (meprobamate)	Chronicity (≤6 mo)	0.26
Initial anxiety score	Initial depression score	0.62
	Initial anger score	0.47
	Initial compulsive score	0.25
	Initial phobic score	0.65
Initial unclassified symptom score	Initial depression score	0.78
	Initial anger score	0.63
	Initial compulsive score	0.58
	Initial phobic score	0.56
Patient's Rx goal (adjustment, psychol Sx, somatic Sx)	Clinic (JHH)	−0.19, 0.23, 0.03
	Initial anger score	0.32, −0.03, −0.25
	Initial comp score	0.18, 0.10, −0.23
	Initial phobic score	0.23, 0.05, −0.17
	Educational level	0.24, −0.05, 0.05
Race (white)	Clinic: JHH	0.30
	Clinic: PGH	−0.34
	Initial anger score	0.24
	Doctor's social class index	−0.34
Marital status (single vs married & widowed)	Clinic (PGH)	0.03, −0.28
	Initial depression score	0.18, −0.25
	Initial phobic score	0.22, −0.10
	Age	−0.27, 0.23
	Sex (male)	0.26, −0.07
	Employed now (no)	0.34, −0.44
	Doctor's discomfort	0.21, −0.12
	Doctor's social class index	0.01, −0.21
Doctor likes patient	Prognosis (fair)	0.25
	Doctor's discomfort	−0.39
Weight	Initial phobic score	−0.21
	Sex (male)	0.34
	Employed now (yes)	0.22
Doctor's drug attitude score	Clinic (JHH)	0.23
	Employed now (yes)	−0.22
	Doctor's discomfort	−0.28
	Residency year (1st)	0.45
	Doctor's social class index	−0.23

teristics of the patient and the treatment situation in the new analyses.

An important methodologic feature of the multiple covariance procedure should be taken into account in further interpreting the findings of the search analysis. The estimated effect of each predictor is adjusted for the estimated effects of all other predictors in the subset selected from the pool. The effects of the selected predictors are not adjusted, however, for the effects of variables not selected from the pool. Table 6 shows the correlations $r > 0.20$ between each predictor selected from the pool and the variables remaining in the pool. These correlations indicate roughly how much the effects of the selected predictors are confounded with the effects of other variables characterizing the patient and the treatment situation.

Inspection of this table reveals that the usefulness of the present sample is limited, for instance by the fact that patients assigned to meprobamate had had shorter illnesses than patients assigned to placebo. Certain characteristics of the patient also are associated with certain characteristics of the doctor. Conventional analyses do not provide information about such associations. Confounding factors, of course, may be present in such analyses even though they are unrecognized.

More detailed consideration of the findings of the search analysis reveals some fa-

miliar themes, as well as some that appear new or unexpected. The observed relationship between relief of anxiety and its initial level, as reported by the patient, is a well-known feature of biological and psychological functions.[5-7] The greater relief experienced by patients who, according to the psychiatric consultant, sought primarily relief of psychological symptoms complements the first finding from another point of view.

The negative prognostic significance of marked somatic complaining appears from the same two viewpoints: the initial score on the cluster of unclassified symptoms on the checklist and the psychiatric consultant's judgment that the patient sought primarily relief of somatic symptoms. Previous controlled studies are in conflict about the significance of somatization. Raab et al[8] found a greater tybamate-placebo difference in patients with a strong tendency to somatize; whereas McNair et al[9] found a greater diazepam-placebo difference in patients without a strong tendency to somatize. In a study of diazepam, phenobarbital, and placebo, Hesbacher et al[10] found the same significant drug-placebo differences in patients with or without a tendency to somatize. The results of the present analysis differ from all the previous studies, but agree with clinical experience, which suggests that somatic preoccupation ordinarily is a poor prognostic sign without respect to treatment.

Apparently neither race nor marital status were investigated previously as predictors of response to minor tranquilizers. Since race in this sample was not related to the usual indices of social class, its effect may depend upon more specific cultural or biological characteristics of the races.

The negative prognostic significance of marriage among patients treated with placebo is somewhat unexpected. Surveys indicate that both the incidence and the duration of psychiatric illness is greater among the unmarried.[11,12]

In this connection, the relationships between marital status and some other variables with prognostic significance are worth noting. Marriage was associated with a low score on the unclassified symptom cluster. However, the reported effect of marriage was adjusted for this favorable bias, since the unclassified symptom score also was se-

lected from the pool as a predictor. On the other hand, the effect of marriage was confounded with the effects of some variables remaining in the pool. The tendency for married patients to be employed represented a favorable bias (Meyer, personal communication). Their low initial depression score represented an unfavorable bias.[13]

Although it is difficult to evaluate the net prognostic contribution of these associated variables to marriage in the patients of this sample, the possibility of an overall negative prognostic effect on this basis alone clearly is present. Different patterns of association among these variables and different statistical adjustments could account for apparent differences between studies in the effect of marriage.

The greater drug-placebo difference reported here for heavier patients also seems paradoxical in a study employing a fixed dose of medication. The effect of weight, however, was confounded with the effect of sex. Heavier patients more often were men. Jenner et al[14] found that men showed a greater drug-placebo difference in response than did women.

In the present study the prognostic significance of weight was most noticeable in patients who received placebo: lighter patients improved more than heavier patients. Patients who received meprobamate improved about the same regardless of weight, and about the same as the lighter patients who received placebo. Thus the combination of heavy weight and placebo treatment was associated with less improvement than the three other possible combinations of weight and treatment. Interactions of this form are typical of many previously reported results with predictor variables.

The greater drug-placebo difference reported here for patients who were liked less by their doctor contradicts an earlier finding by Rickels et al.[15] They found that patients who were liked by their doctor showed a greater drug-placebo difference in response than patients who were disliked by their doctor. This contradiction raises the question whether the doctor's attitude toward the patient in Rickels's study may have been confounded, for example, with the doctor's attitude toward the medication.

In the present analysis, the effect of each of these two variables is adjusted for the effect of the other. This adjusted result is more in accord with the findings on the therapist's warmth by the client-centered therapists. According to a review by Truax and Carkhuff,[16] patients who are offered higher levels of warmth by their therapist improve more. The doctor's dislike presumably interferes with his ability to offer warmth and so constitutes a negative factor in treatment. It is not surprising that patients who receive lower levels of an important psychotherapeutic ingredient stand to gain more from medication.

In their review, Uhlenhuth et al[17] pointed out that studies on predictors of drug response identified certain characteristics of the patient, the treatment situation and the life situation with unfavorable implications for improvement in psychoneurotic outpatients. The effectiveness of minor tranquilizers as compared to placebo seemed particularly apparent in the presence of these poor prognostic indicators.

This impression is supported by the present findings in regard to marital status, weight, and the doctor's attitude toward the patient. (The pharmacologic effect of the drug in the present study does not significantly modify the effects of some other negative prognostic factors, however, such as a high initial level of unclassified symptoms.) From another viewpoint, drug therapy apparently evokes no additional improvement if other prognostic factors are favorable.

The doctor's attitude toward drugs probably does not share the broad prognostic significance of the three variables discussed above. In the present study, however, doctors with a more favorable attitude toward drugs generally were less experienced, first-year residents. To this extent, the doctor's drug attitude may carry some prognostic significance through confounding with his experience.

The importance of the doctor's attitude toward drug therapy in modifying the patient's observed response to medication was pointed out by Feldman as long ago as 1956.[18] Studies with neurotic patients by Kast and Loesch[19] and by Uhlenhuth et al[20] suggested the same phenomenon. The subsequent literature on this point contains conflicting reports.[17] These conflicts also may depend in part upon different degrees of confounding between the doctor's attitude toward medication and toward the patient.

A methodologic feature of most controlled studies also bears on the interpretation of results on this area. The double-blind protects against the exaggeration of minor differences between treatments by the enthusiastic observer. This device, however, does not protect against the suppression of significant differences between treatments by the unenthusiastic observer. It is only necessary for him to rate all subjects as equally improved.

The effect of the observer's attitude toward drugs on the rating process, therefore, may be confused with the effect of the doctor's attitude toward drugs on the patient's actual response to medication. Disagreement among studies, then, may depend in part upon differences in the sensitivity of their criterion measures to the kind of bias described above.[21]

The foregoing discussion underlines the conceptual and interpretative problems which indeed are evident throughout this report. The approach presented here, although it offers no easy solutions, brings into sharper focus the problems inherent in all research conducted in a complex field of interrelated influences. The shifting patterns of association among variables in such a field from one sample to another lead to shifts in the predictors identified as most important. Such shifts, even though not statistically significant, complicate interpretation.

Several strategies for coping with these problems suggest themselves. Perhaps the most straightforward is to repeat studies with many independent variables until sufficient information is available to reach consensus on the most important predictors.

Alternatively, for the sake of conceptual simplicity, a smaller set of independent variables can be selected for repeated studies. This procedure may be slower in the long run because fewer variables are examined and because there is greater opportunity for confounding with variables outside the selected set.

A third strategy begins with reducing the field of correlated independent variables to a few groups of related variables by means of

factor analysis. The effects of these relatively uncorrelated factors on the criterion then can be investigated with the approach presented in this paper. The instability of the factor structures across samples of the size usually available may present problems as serious as those discussed earlier. In addition difficulty in interpreting empirically defined factors in clinically significant terms can arise.

While all of these approaches may be worth trying, clearly none of them offer ready answers. For precise results in the face of relatively imprecise data, all of these approaches require the laborious accumulation of large amounts of data. Meanwhile, how can the tentative results currently available help the clinician with his daily problems in selecting "the right drug for the right patient"?[22]

Given the appropriate measures of the characteristics of the patient and the treatment situation presented above (and their availability presents a large "if"), a new patient's responses both to meprobamate and to placebo could be estimated with the constants and coefficients presented in the analysis of variance table. The selection of treatments for patients by this method has been simulated in a research setting.[23] This method is not yet ready for general clinical application, however, nor would most clinicians find such a mechanical approach attractive.

It is worth noting again that only four of the predictor variables presented bear on the choice between meprobamate and placebo treatment. In summary the heavier male married patient who is less well liked by his doctor benefits most from the active drug. Conversely, the slim single woman who is well liked by her doctor benefits least from the active drug, partly because of her strong positive response to placebo. These criteria the clinician can apply readily. Furthermore, the doctor who favors drug therapy is more likely to realize the potential benefit of the medication. Finally, even when all four differential predictors are unfavorable to meprobamate, the patient's predicted response to the drug is *no worse* than to placebo. It would be unwise, of course, to generalize these reassuring conclusions beyond the conditions of the present study, which deals specifically with psychoneurotic patients, anxiety symptoms, and meprobamate.

Summary

The purpose of this study was to identify the characteristics of anxious outpatients and the treatment situation associated with relief of anxiety in response to meprobamate. A total of 138 psychoneurotic outpatients manifesting anxiety were treated for six weeks with medication and brief, supportive interviews every two weeks with a psychiatric resident. Patients received either meprobamate 400 mg, q.i.d., or an identical placebo under double-blind conditions.

Patients reported their symptomatic condition before each interview on a checklist of 64 common symptoms. The checklists were scored in terms of six symptom clusters, including anxiety, developed on the basis of clinical judgment.

The change in the patients' anxiety scores across the six weeks of the study was analyzed in relation to the simultaneous effects of medication, 29 other characteristics of the patients and their treatment situation, and the interactions between medication and these 29 other characteristics. A specially developed multiple covariance procedure with a search option, programmed for the IBM 7094, was used.

The full set of variables accounted for about $R^2 = 74\%$ of the variation in the criterion, with an overall F-ratio of 2.301 and a computed p of 0.002.

The stepwise search procedure revealed that the greatest relief of anxiety, irrespective of medication, was experienced by the more anxious Negro patient with less somatic symptomatology, who sought relief of psychological symptoms, rather than psychological readjustment or relief of physical symptoms.

The heavier male married patient who was less well liked by his doctor benefited most from the active drug, as compared to placebo. Conversely, the slim single woman who was well liked by her doctor benefited least from the active drug, partly because of her strong positive response to placebo.

Finally, even when all four differential predictors of drug effect were unfavorable to meprobamate, the predicted response of the patient's anxiety to the drug was no worse than to placebo.

Generic and Trade Names of Drugs

Meprobamate—*Equanil, Miltown.*
Diazepam—*Valium.*
Phenobarbital—*Luminal.*

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