Articles

A Randomized Double-Blind Study of the Effect of Distant Healing in a Population With Advanced AIDS

Report of a Small Scale Study

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A recent editorial called for "the scientific community to stop giving alternative medicine a free ride" (Angell M, Kassirer JP. Alternative medicine: the risks of untested and unregulated remedies. N Engl J Med 1998; 339:841). We agree. Now is the time for scientists to be courageous, as well as careful and precise, to help separate truth from hope and fact from myth. The paper published below is meant to advance science and debate. It has been reviewed, revised, and re-reviewed by nationally known experts in biostatistics and in complementary medicine. It reports a 6-month blinded study of 40 patients with AIDS who knew they might receive distant healing treatments representing a variety of traditions. Patients who received treatment had a statistically significant more benign course than control subjects. Does the paper prove that prayer works? No. The authors call for more research, as do we and the reviewers, for a number of reasons. We note that the study was relatively short and analysed rather few patients. No treatment-related mechanisms for the effects were posited. The statistical methods can be criticized. We have chosen to publish this provocative paper to stimulate other studies of distant healing and other complementary practices and agents. It is time for more light, less dark, less heat.

—Linda Hawes Clever, MD
Editor

Various forms of distant healing (DH), including prayer and "psychic healing," are widely practiced, but insufficient formal research has been done to indicate whether such efforts actually affect health. We report on a double-blind randomized trial of DH in 40 patients with advanced AIDS. Subjects were pair-matched for age, CD4+ count, and number of AIDS-defining illnesses and randomly selected to either 10 weeks of DH treatment or a control group. DH treatment was performed by self-identified healers representing many different healing and spiritual traditions. Healers were located throughout the United States during the study, and subjects and healers never met. Subjects were assessed by psychometric testing and blood draw at enrollment and followed for 6 months. At 6 months, a blind medical chart review found that treatment subjects acquired significantly fewer new AIDS-defining illnesses (0.1 versus 0.6 per patient, $P = 0.04$), had lower illness severity (severity score 0.8 versus 2.65, $P = 0.03$), and required significantly fewer doctor visits (9.2 versus 13.0, $P = 0.01$), fewer hospitalizations (0.15 versus 0.6, $P = 0.04$), and fewer days of hospitalization (0.5 versus 3.4, $P = 0.04$). Treated subjects also showed significantly improved mood compared with controls (Profile of Mood States score –26 versus 14, $P = 0.02$). There were no significant differences in CD4+ counts. These data support the possibility of a DH effect in AIDS and suggest the value of further research.

(Sicher F, Targ E, Moore D, Smith HS. A randomized double-blind study of the effect of distant healing in a population with advanced AIDS—report of a small scale study. West J Med 1998; 169:356–363)

Distant healing (DH) is defined as a conscious, dedicated act of mentation attempting to benefit another person's physical or emotional well-being at a distance. Various forms of DH, including prayer and some forms of spiritual healing, are widely reported and subscribed to in the United States.[1,2] Anecdotal experience with DH has

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ABBREVIATIONS USED IN TEXT

ADD = AIDS-defining disease
BHS = Boston Health Study
DH = distant healing
MOS = Medical Outcomes Survey for HIV
POMS = Profile of Mood States
WPSI = Wahler Physical Symptom Inventory

stimulated a substantial body of research including at least 131 laboratory-published studies reviewed by Benor,[3] of which 56 found significant effects. Many of the studies, however, lacked rigorous control, measured only responses *in vitro,* involved only brief periods of influence, or did not include extended follow-up. The medical literature does contain a report of a rigorously controlled clinical study by Byrd,[4] who investigated the effects of intercessory prayer for 383 patients sequentially admitted to the San Francisco General Hospital Coronary Care unit. The study reported a significant improvement in hospital course and decreased medical complications in the treated group, but the period of medical follow-up was limited to the time each subject spent in the hospital, so delayed effects were not studied. In addition, outcome measures were not predefined. Thus, the longer-term efficacy of DH remains unstudied, and additional, scientifically rigorous studies are required to establish whether DH can be an effective intervention for life-threatening disease.

For these reasons, and without having conducted any previous DH studies at all, we chose to evaluate DH in a population of advanced AIDS patients with 6-month follow-up. Our initial study was a double-blind pilot study of 10 treated and 10 control subjects conducted during July 1995 through January 1996. The pilot study suggested both medical and psychological benefits of distant healing. Four of the 10 control group subjects died, with no deaths occurring in the treatment group, but the result was confounded by age (those who died were older). As a result, in the second larger study (reported here in full) a pair-matched design was used to control for factors shown to be associated with poorer prognosis in AIDS,[5] specifically age, T cell count, and illness history. Additionally, an important intervening medical factor changed the endpoint in the study design. The pilot study was conducted before the introduction of "triple-drug therapy" (simultaneous use of a protease inhibitor and at least two antiretroviral drugs), which has been shown to have a significant effect on mortality.[6] For the replication study (July 1996 through January 1997, shortly after widespread introduction of triple-drug therapy in San Francisco), differences in mortality were not expected and different endpoints were used in the study design. Based on results from the pilot study, we hypothesized that the DH treatment would be associated with *1*) improved disease progression (fewer and less severe AIDS-defining diseases [ADDs] and improved $CD4^+$ level), *2*) decreased medical utilization, and *3*) improved psychological well-being. The results of this replication study are reported below.

Subjects and Methods

Forty subjects were recruited by distributing fliers at clinics and at AIDS-related events and through advertisements in both gay and mainstream newspapers in the San Francisco Bay Area. Efforts were made to reach a wide range of socio-demographic populations. All subjects were required to meet the criteria of the Centers for Disease Control AIDS category C-3 ($CD4^+$ cell count <200 cells/μl, history of at least one ADD)[7] and to be taking *Pneumocystis carinii* pneumonia prophylaxis. Subjects signed informed consent, were photographed, and were randomly assigned on a double-blind basis to either DH or a control group. Subjects were told they had a 50-50 chance of receiving the DH treatment. Both groups continued to receive standard medical care at their primary care sites. Subjects were pair-matched by age, $CD4^+$ count, and number of ADDs before randomization.

Data acquisition

Subjects came to the laboratory or were visited at home to complete baseline and repeated measures at enrollment, at the end of the 10-week treatment intervention, and at follow-up 12–14 weeks later (Fig. 1). Measurements taken were $CD4^+$ count, psychological distress as measured by the Profile of Mood States (POMS),[8] physical symptoms as measured by the Wahler Physical Symptom Inventory (WPSI),[9] and quality of life as measured by the Medical Outcomes Survey (MOS) for HIV.[10] In addition, subjects reported doctor visits, hospitalizations, illness recovery, and onset of new illnesses. To verify the report, 6 months from the start of the study a blind medical chart review was performed by a study physician who catalogued outpatient doctor visits, hospitalizations, and remission or development of ADDs over the study interval. The review was done at 6 months only because of the focus of the study on extended treatment effects. Additional variables included subject's belief in the efficacy of DH, years HIV-positive, previous ADDs, protease inhibitor use, triple-drug therapy use, site of medical care delivery, use of complementary health practices, social support for study participation, drug and alcohol use, and demographics. Subjects were also asked, in a self-administered questionnaire, which group they thought they were in, treatment or control. For the one subject who died near the end of the study, all data were collected except the final $CD4^+$ count.

Evaluation of illness severity

To control for the variation in severity and prognosis of different AIDS-related illnesses, all illnesses were scored according to the Boston Health Study (BHS) Opportunistic Disease Score,[11] which includes both AIDS-defining and secondary AIDS-related diseases. The BHS severity scoring system has been validated in predicting survival in two large populations of AIDS patients. New ADDs were counted as "ADDs acquired" only if blind chart review revealed no prior diagnosis of the condition; the only exception to this rule was Kaposi's sarcoma. Because cutaneous Kaposi's sarcoma

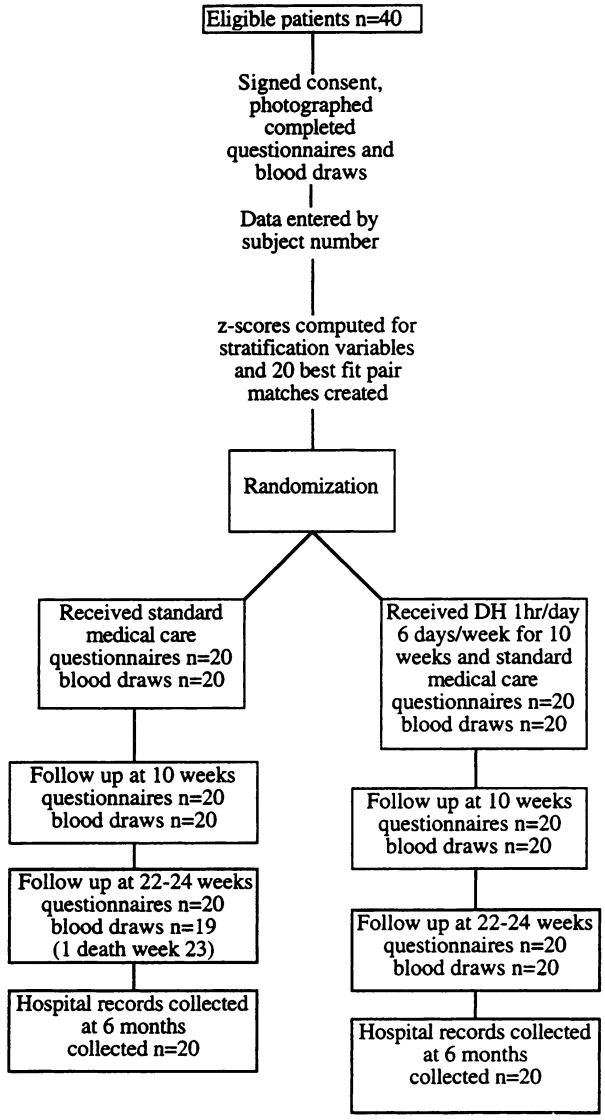

Figure 1.—Study flow chart.

is scored in a different severity category than visceral Kaposi's sarcoma, patients progressing from cutaneous to visceral Kaposi's sarcoma were counted as having acquired a new illness. Relapsing and remitting opportunistic diseases such as thrush or herpes or non–AIDS-defining bacterial infections were counted only once, whether or not there were recurrences. Recoveries from ADDs were tabulated when subjects' medical charts specifically stated a recovery had occurred or that there had been no evidence of the illness for at least 3 months.

Pair matching

Pair matching was done to control as much as possible for variation in outcomes that might be related to major disease progression and survival predictors, as indicated by the pilot study and in the medical literature.[6,11] The variables were age, baseline CD4+ (T cell) count, and history of ADDs (sum of previous and current ADDs). These three variables were used to form matched subject pairs. First, a normalized z score was computed for each subject for each variable by subtracting the mean for all subjects and dividing the result by the standard deviation for all subjects. Next, all pairwise sums-of-squared differences in z scores between subjects (over the three variables) were computed. For each subject, an average difference from all the other subjects was calculated. Starting with the subject with the largest average difference, the closest match was found. The two matched subjects were eliminated from the list and the procedure was iterated until all 40 subjects were paired. A computer-generated binary random number was then used to randomly assign one member of each pair to treatment and one to control.

Blinding procedures

All subject enrollment interviews were performed by one of two staff members who assigned subjects enrollment numbers. After enrollment was complete, a third staff member used a random number table to assign "study code" numbers to each of the enrollment numbers; these were substituted in the computer and used in randomization. Medical charts were obtained at the end of the study; names were removed from all text, and charts were assigned a new set of code numbers before they were reviewed. The chart reviewer did not know which subjects were in which group at the time of review. All data were entered into the computer by a research assistant who was blind to group assignment. Subjects learned their group assignment 1 year after the the study ended.

Treatment procedures

At the time of enrollment all subjects were photographed, and subject information packets including 5×7-inch color photograph, first name, CD4+ count, and current symptoms were prepared by a research assistant. Ten copies of each packet were made and marked with removable labels indicating the subject's enrollment number. After randomization, the enrollment numbers were removed from the packets and replaced with the study codes. The packets were then divided into treatment and control groups based on the randomization results. Control subject packets were retained unopened in a locked file drawer. Treatment subject packets were grouped in batches of five to be sent to each healer. Each of the five envelopes sent to the healers was marked with the day to be opened to begin the healing period for that patient.

Healers

Forty DH practitioners, including 12 from the pilot study, were recruited via professional healing associations and schools of healing. Eligibility criteria were minimum 5 years regular ongoing healing practice, previous healing experience *at a distance* with at least 10 patients, and previous healing experience with AIDS.

Healers had an average of 17 years of experience and had previously treated an average of 106 patients at a distance. Practitioners included healers from Christian, Jewish, Buddhist, Native American, and shamanic traditions as well as graduates of secular schools of bioenergetic and meditative healing. Practitioners were not paid and understood that the study could not evaluate the abilities of any individual practitioner. Healers were residing at various locations throughout the United States. The site from which they performed their healing was not restricted.

Healing treatment

A rotating healing schedule randomized healers to subjects on a weekly basis to minimize possible differences in healer effectiveness. Thus, each subject in the DH group was treated by a total of 10 different practitioners, while each practitioner worked every other week treating a total of 5 subjects. Each healer received five consecutively numbered subject information packets with instructions specifying the day to begin treatment on each subject. Healers were asked to work on the assigned subject for approximately 1 hour per day for 6 consecutive days with the instruction to "direct an intention for health and well-being" to the subject. Healers completed logs for each healing session, indicating period of healing, specific technique, and any impressions of the subject's illness. Subjects never met practitioners and did not know whether they were in the DH group, where the practitioners were located, nor at what time the DH might occur. Before the intervention, study personnel encouraged and motivated healers via letters and phone calls stressing the importance of the study and their individual efforts.

Statistical methods

Baseline and outcome comparisons between the two groups involved three statistical tests: paired t test for all continuous or multilevel variables, Wilcoxon signed-rank test when the data appeared to be skewed or contained outliers, and McNemar's test for 2×2 tables comparing paired binary variables. For study outcomes where $P < 0.05$, since many of the outcomes had skewed or clumped distributions (caused by tied values in outcome), a randomization test[12] was also used to obtain an "exact" P value for the observed outcome.

In addition, because study outcomes may be correlated, Hotelling's T-square statistic was used to determine whether there was a treatment effect on the array of 11 medical and psychological outcomes. Again, since this statistic assumes multivariate normality of the outcomes (which is not the case), statistical significance of the outcome array was further assessed by conducting a randomization test on the T-square statistic. A randomization test is based on comparing a set of observed outcomes with those generated by randomly permuting the treatment-control assignment of subjects. Randomization tests are distribution free, that is, no assumption concerning the distribution of the test statistic is required. In this way, an unbiased determination of significance is obtained without assumptions concerning the distribution of the test statistic. (An informative discussion of randomization tests in a medical setting is contained in a recent issue of *The American Statistician.*[13]) This method for determining statistical significance was necessitated by the nature of the outcomes data.

We also examined the effects of differences in baseline factors (those with two-sided $P < 0.2$) on outcome variables by stratifying on levels of baseline factor when they were discrete and by analysis of covariance when they were continuous.

Results

Baseline comparisons

Subjects were 37 men and 3 women with a mean age of 43 (Table 1). Only one patient (DH group) had a history of intravenous drug use. There were no statistically significant differences on any baseline measures between the treated and control groups, including those used for pair-matching, or in ongoing AIDS management-related variables, such as use of triple-drug therapy (Table 1). There were several near-significant differences ($P < 0.20$), however. All five baseline smokers and all four minorities were in the control group ($P = 0.06$ and $P = 0.12$, respectively). Of note, two treated subjects resumed their smoking habit during the study period (one near the beginning and one near the middle), reducing group smoking differences. The control group also was HIV-positive for a shorter time (7.3 versus 9.0 years, $P = 0.11$), showed a trend toward lower initial psychological distress scores (POMS 43 versus 62, $P = 0.19$), and had used fewer alternative therapies (2.7 versus 4.2, $P = 0.10$).

A review of primary care sites found no significant differences in site or type of medical practice (university, specialty clinic, solo practice). Review of charts, each containing complete medical history, found no major comorbid conditions (heart disease, cancer, diabetes) in either group. A majority of subjects (85%) expressed an *a priori* belief in the benefit of DH. The level of belief at baseline was nearly equal for both groups, and the belief showed no correlation with medical outcomes.

Medical and psychosocial outcomes

Over the 6-month study period, the DH group experienced significantly fewer outpatient doctor visits, fewer hospitalizations, fewer days of hospitalization, fewer new ADDs, and a significantly lower illness severity level as defined by the BHS scale (Table 2). All diseases acquired are listed in Table 3. At 6 months, the DH group also showed significantly improved mood compared with controls as measured by the POMS, reflecting improvement on four of six subscales (depression, $P < 0.02$; tension, $P < 0.02$; confusion; $P < 0.002$; fatigue, $P < 0.02$). Differences on the WPSI and MOS were not significant between groups. One death occurred in the control group, after the patient's follow-up questionnaire had

TABLE 1.—*Baseline and AIDS Management-Related Variables*

n	*Treated* 20	*Control* 20	*Two-sided P*[1]
Age (years)	42.9 ± 7.2	43.2 ± 6.4	0.80
Sex (% female subjs.)	10	5	1.00
Ethnic minority (% subjs.)	0	20	0.12
Education[2]	4.1 ± 0.6	3.9 ± 1.0	0.38
Baseline AIDS-related factors			
Years HIV positive	9.0 ± 3.5.	7.3 ± 3.1	0.11
CD4 cell number/ml	90.3 ± 66.0	83.8 ± 70.9	0.55
No. existing ADDs	1.4 ± 1.3	1.3 ± 1.4	0.65
No. prior ADDs	1.9 ± 1.3	2.1 ± 1.4	0.58
ADD severity[3]	5.4 ± 3.0	5.0 ± 3.3	0.49
Interventions during study			
Triple-drug therapy[4]			
Throughout study	70	80	0.72
At least 2 months	20	15	1.00
Protease inhibitors	90	95	1.00
Pneumonia carinii prophylaxis	100	100	1.00
No. alternative therapies[5]	4.2 ± 2.6	2.7 ± 2.0	0.10
Support[6]	85	95	0.61
Psychotherapy	45	50	1.00
Baseline subjective measures			
WPSI score	1.64 ± 0.72	1.69 ± 0.80	0.86
POMS score	62.3 ± 46.7	42.8 ± 39.9	0.16
MOS score[7]	−0.01 ± 0.8	−0.01 ± 0.8	1.00
Baseline personal habits			
Smokers	0	25	0.06
Recreational drug use[8]	20	20	1.00
Alcohol use[9]	0.4 ± 0.6	0.8 ± 1.1	0.27
Exercise[10]	1.4 ± 1.3	1.9 ± 1.4	0.34
Meditation practice	60	75	0.50
Religious/spiritual practice	90	80	0.66
Belief in DH[11]	2.8 ± 0.6	2.9 ± 0.4	0.33

Data are means ± SD or %.
[1]Paired *t* test for continuous variables, Wilcoxon signed-Rank test for variables with outliers, McNemar's test for binary variables; all tests are of matched paired differences. "Matched" refers to variables used for pair matching.
[2]Some high school = 1, high school graduate = 2, some college = 3, college graduate = 4, graduate degree = 5.
[3]Boston Health Study opportunistic disease score.
[4]Simultaneous use of a protease inhibitor and at least two antiretroviral drugs.
[5]Acupuncture, psychic healing or prayer, Chinese herbs, yoga, biofeedback, guided imagery, Chi Gong, nutritional supplements or vitamins, special diet, group therapy, or other.
[6]Number of subjects reporting study participation support from family or community members.
[7]Normalized mean score for 10 factors.
[8]Four subjects in each group used crack cocaine or oral amphetamines; one treatment subject also used IV amphetamines.
[9]No alcohol = 0, once or twice a week = 1, several times a week = 2, heavily on weekends = 3, daily = 4.
[10]No exercise = 0, once a week = 1, two or three times a week = 2, four or five times a week = 3, daily = 4.
[11]"I doubt it" = 0, "Maybe" = 1, "Probably" = 2, "Yes, definitely" = 3.

been completed but 1 week before the 6-month study endpoint. There was a nonsignificant trend toward increase in $CD4^+$ count for both groups, although the two groups did not differ significantly on this measure. Thus, the DH treatment was associated with significantly better outcomes on 6 of the 11 medical outcome measures.

At study midpoint, immediately after the treatment intervention, subjects were asked if they thought they had been in the DH or control group. Two subjects (one from each group) did not respond. Nine of the DH group subjects and 13 of the control group subjects believed they were in the DH group ($P = 0.32$; Fisher's exact test). Additional analysis was done to investigate possible correlation between subject belief about group assignment and study outcomes. Belief about group assignment did not correlate with any study outcome except $CD4^+$ change ($P = 0.05$). This correlation no longer held when subjects were again asked to guess group assignment at the end of the 6-month study period ($P = 0.28$). At the end of the study period, subjects who had experienced more recoveries did tend to correctly guess they had been in the treatment group ($P = 0.05$).

TABLE 2.—*Medical Course Over 6-Month Study*

Medical Outcome	*Treated (n = 20)*	*Control (n =20)*	*Two-tailed P*[1]
Outpatient visits	185 (9.2 ± 5.9)	260 (13.0 ± 7.0)	0.01
Hospitalizations	3 (0.15 ± 0.5)	12 (0.6 ± 1.0)	0.04
Days of hospitalization	10 (0.5 ± 1.7)	68 (3.4 ± 6.2)	0.04
Illness severity[2]	16 (0.80 ± 1.15)	43 (2.65 ± 2.41)	0.03
ADDs acquired	2 (0.1 ± 0.3)	12 (0.6 ± 0.9)	0.04
ADD recoveries	6 (0.3 ± 0.6)	2 (0.1 ± 0.3)	0.23
$CD4^+$ change (/μl)[3]	31.1 ± 54.9	55.5 ± 102.0	0.55
Deaths	0	1	1.00
Change in POMS score (distress)	−25.7 ± 46.0	14.2 ± 49.0	0.02
Change in MOS	0.2 ± 0.8	−0.2 ± 0.8	0.15
Change in WPSI	−0.2 ± 0.6	0.1 ± 0.9	0.31

Data are *n* (means ± SD) or means ± SD.

[1]Wilcoxon signed-rank test for the first seven outcomes; paired *t* tests for the last three outcomes; McNemar's test for number of deaths. Due to clumpiness of the data for variables near $P = 0.05$, the randomization test was also performed with the following results: hospitalizations, $P = 0.06$; days of hospitalization, $P = 0.04$; ADD severity score, $P = 0.03$; ADDs acquired, $P = 0.06$.

[2]Boston Health Survey opportunistic disease severity score, includes ADD and AIDS-related illness (Table 3).

[3]n =19 in the control group (one subject died).

Baseline effects on outcomes

Where baseline group differences were near-significant ($P < 0.20$), these variables were examined for correlation with all study outcomes. We found no effects of the baseline differences in smoking, number of years HIV-positive, or number of alternative therapies used on any outcomes. As described above, the treatment group tended to have higher baseline POMS scores (more distress) than controls. Higher baseline psychological distress, in both groups, was significantly correlated with greater reduction in psychological distress at the end of the study ($P < 0.001$). When baseline POMS was used as a covariate to adjust the POMS change scores, the difference in POMS change scores switched from statistical significance in favor of the treated to significance in favor of the controls. Baseline POMS values did not significantly correlate with any of the medical outcomes, although, as expected, they did correlate with the other psychological measures.

Minority status (with all 4 minorities in the control group) showed a near-significant difference at baseline. When this variable was examined *within* the control group (4 minorities versus 16 nonminorities), no significant correlation with study outcomes was found. However, a stratified analysis on all subjects, which takes minority differences in treatment-control pairs into account, resulted in a change in the P values from 0.04 to 0.09 for number of hospital stays and from 0.04 to 0.08 for number of hospital days. The difference in minority status among treated and control did not significantly correlate with any other outcome variable.

Analysis of Outcome Array

Many of the outcomes in Table 2 are correlated with each other. Thus, it is useful to evaluate the treatment effect by using a statistic that takes into account these correlations. The results of the randomization test applied to Hotelling's T-square statistic indicated that the array of all outcomes is statistically significant ($P = 0.0154$; that is, in the 10,000 random samplings only 154 T-squares exceeded the observed Hotelling T-square statistic).

Discussion

The findings of decreased medical utilization, fewer and less severe new illnesses, and improved mood for the treated group compared with the controls supports a positive therapeutic effect of DH. This outcome is difficult to explain, particularly in this double-blind study where subjects, physicians, and study personnel did not know who was in the treatment group. There are two explanations other than a DH effect that, in principle, could explain these data.

First, differences between the group outcomes might be attributed to baseline medical or treatment differences. This possibility was not supported by univariate comparison of baseline AIDS-related variables, as shown in Table 1, where there were no statistically significant differences between the groups. Detailed analysis of baseline variables differing at $P < 0.20$ did find that higher baseline POMS scores were associated with greater improvement in POMS scores over the course of the study. By chance, patients in the treatment group showed more psychological distress at baseline, so their improved mood over the study interval may represent simply an effect of increased hope or expectation due to their participation in an intervention research study. The additional finding that adjusting for differences in baseline POMS caused a change in the direction of the beneficial effect is difficult to understand and is likely due to chance.

While baseline psychological state, as measured by the POMS, did correlate with psychological outcomes, it did not correlate with any of the medical outcomes. Detailed

TABLE 3.—*Distribution of AIDS-Related Illnesses Acquired During the Study*

n	*Treated* 20	*Control* 20
BHS severity group III (ADD)		
Kaposi's sarcoma (visceral)	0	1
Mycobacterium avium complex	1	1
BHS severity group II (ADD)		
Cytomegalovirus	0	2
HIV encephalitis	0	1
Coccidiomycosis	0	1
Wasting syndrome	0	1
Pneumocystis carinii pneumonia	1	1
BHS severity group I (ADD)		
Esophageal candidiasis	0	2
Kaposi's sarcoma (cutaneous)	0	1
Recurrent pneumonia	0	1
BHS severity group I (AIDS-related)		
Pseudomonas sepsis	0	1
Meningitis sepsis	0	1
Oral leukoplakia	0	1
Kaposi's sarcoma metastasis (cutaneous)	0	1
Renal insufficiency	0	2
Oral thrush	1	5
Herpes (genital/rectal)	1	3
Oral ulcers	1	0
Anemia	3	1
Bacterial infection	5	8
AIDS-related illnesses not scored by BHS		
Cervical dysplasia	1	2
Diarrhea	2	6
Peripheral neuropathy	5	6

Data are number of cases; presence or absence was based on blind medical chart review.

examination of the effects of differences in baseline factors on outcomes also found a marginal effect of difference in minority status for hospitalizations. This is an interesting finding but is weakened by the fact that in this study no minorities received DH. In fact, when hospitalizations and hospital days are examined within the control group alone, ethnicity does not make a significant difference. Because our sample of minorities was so small and they all ended up in the control group, the fact that they had proportionately more hospitalizations is very hard to interpret. Adjustment for their contributions has only a small effect on the *P* value, but clearly a larger sample with more minorities would be required to determine whether DH was affecting hospitalizations. It is important to point out that having conducted 50 statistical tests to find interactions between differences in baseline factors and outcomes (excluding death), only two were found, which is the number expected by chance. We found no baseline differences with $P < 0.20$, which could explain differences in number of doctor visits or number or severity of new ADDs. Although there was a near-significant trend for more smokers in the control group, by the study midpoint treatment subjects who resumed smoking brought the distribution into better balance. There was no correlation with smoking status and any study outcome. It does remain possible, however, that combinations of baseline variables or differences in some unmeasured variable may have influenced outcomes.

A second possible explanation for the data is an expectation or placebo effect, as when patient improvement occurs due to a belief about the effectiveness of a treatment.[14,15] This is especially worth examining given the finding that baseline psychological status may have affected change in psychological well-being during this study. The expectation effect should lead to better outcomes among subjects who believe they were in the treatment group, regardless of their true group assignment. Differences in medical outcomes were related to true group assignment, however, and unrelated to assignment belief. The only outcome measure showing correlation with subject belief was $CD4^+$ count, and interestingly, this finding held up only at the study midpoint and not at the end of the study. Possibly, early in the study, subjects who believed they were in the treatment group came to this belief because they knew from some other source that their $CD4^+$ count was rising. We cannot eliminate the possibility that hope or expectation as reflected by the subject's guess may have affected $CD4^+$ count, but $CD4^+$ count did not differ between the two study groups, so it does not seem likely this factor affected the differential study outcomes.

The findings of reduction in medical utilization and development of fewer and less severe new illnesses suggest, as in the Byrd study, a global rather than a specific DH effect. This study made an initial attempt to identify a specific marker of DH action by including $CD4^+$ counts. Despite the differences in medical morbidity, however, there were no significant differences between the groups in $CD4^+$ counts, which generally remained very low. Recent evidence suggests that viral load may be a better outcome predictor than $CD4^+$ count.[16] Future studies should seek specific markers of DH effect with viral load and natural killer cell activity.

Existing medical understanding offers no mechanism to account for a finding of healing at a distance; however, science does not require a known mechanism to prove the existence of a phenomenon. As pointed out by Dossey,[17] for years no one knew how colchicine, morphine, aspirin, or quinine worked, yet they were known to be effective. Hand-washing, too, became standard medical practice well before a theory of infectious disease was described. Possible mechanisms for DH might include some form of mind-to-mind communication between patient and practitioner or some form of previously undescribed energy transfer. Such concepts are, of course, highly speculative and remain an area for future research.

The finding of reduced medical utilization and improved medical course in the DH group is both exciting and surprising, but it remains crucial for this work to be replicated to be more confident that the effect is real.

If the effect is robust, future studies will also need to compare different DH techniques and investigate the efficacy of DH in different illnesses and with different subject populations.

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