ORIGINAL ARTICLE

The Ability of Multifamily Groups to Improve Treatment Adherence in Mexican Americans With Schizophrenia

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Context: Evidence-based interventions to improve medication adherence among patients with schizophrenia are lacking. Although family psychoeducation has demonstrated efficacy in improving outcomes in schizophrenia, empirical support for its ability to enhance medication adherence is scarce.

Objective: To determine whether a culturally adapted, multifamily group (MFG) therapy would increase medication adherence and decrease psychiatric hospitalizations for Spanish-speaking Mexican Americans with schizophrenia.

Design: A total of 174 Mexican American adults with schizophrenia-spectrum disorder and their key relatives were studied in a 3-armed, randomized controlled trial of MFG therapy focused on improving medication adherence. Assessments occurred at baseline and at 4, 8, 12, 18, and 24 months.

Setting: Two community mental health centers in Los Angeles, California.

Participants: Patients had a diagnosis of schizophrenia or schizoaffective disorder with a recent exacerbation of psychotic symptoms and nonadherence to medication before enrollment.

Intervention: Patients participated in 1 of 2 MFGs (MFG-adherence or MFG-standard) or treatment as usual. Groups convened twice monthly in 90-minute sessions for 1 year.

Main Outcome Measures: The Treatment Compliance Interview uses multiple sources of information to quantify medication adherence. Computerized records were used to collect information on the use of inpatient resources.

Results: At the end of the 1-year treatment, MFG-adherence was associated with higher medication adherence than MFG-standard or treatment as usual only ($F=6.41$; $P=.003$). The MFG-adherence participants had a longer time to first hospitalization ($\chi^2=13.3$; $P=.001$) and were less likely to be hospitalized than those in MFG-standard ($\chi^2=8.2$; $P=.04$) and treatment as usual alone ($\chi^2=11.3$; $P<.001$). Increased adherence accounted for one-third of the overall effect of treatment on the reduced risk for psychiatric hospitalization.

Conclusion: Multifamily group therapy specifically tailored to improve medication adherence through a focus on the beliefs and attitudes of the target population is associated with improved outcome for Mexican American adults with schizophrenia-spectrum disorders.

Trial Registration: clinicaltrials.gov Identifier: NCT01125267

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MANY INDIVIDUALS WITH schizophrenia do not adhere to their antipsychotic medication regimens,[1] resulting in disproportionate use of costly inpatient services and poorer long-term outcomes.[2,3] This is an important and costly public health issue, especially among Mexican Americans with schizophrenia,[4,5] because treatment nonadherence approaches 60% in this population.[6] The Surgeon General's report ("Mental Health: Culture, Race, and Ethnicity") noted, "The system of mental health services currently in place fails to provide for the vast majority of Latinos in need of care."[7(p146)]

Given that Hispanics have become the largest ethnic minority population in the United States and that Mexican Americans make up well over 60% of the Hispanic population,[8] the paucity of evidence-based practices designed to overcome the barriers to continuous treatment for this group represents a critical, unmet need. We report on a family intervention that addresses medication nonadherence in Spanish-speaking Mexican Americans with schizophrenia. We chose a family approach because living with supportive rela-

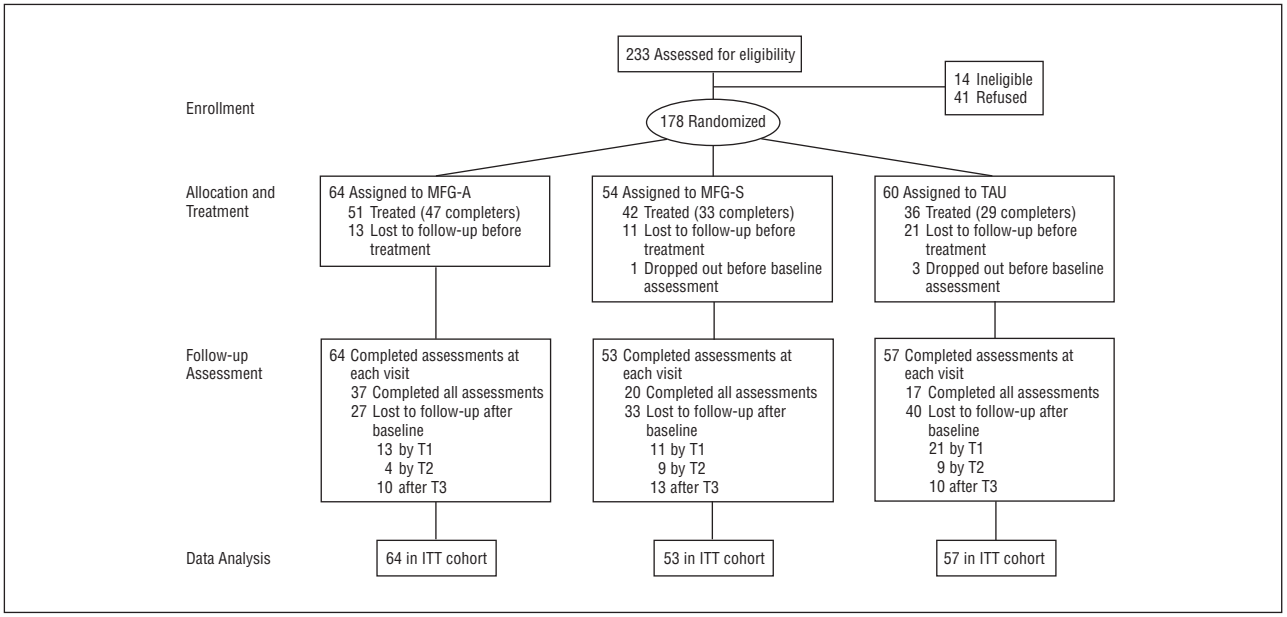

Figure 1. Randomized trial flow diagram. ITT indicates intention-to-treat; MFG-A, multifamily group-adherence; MFG-S, multifamily group-standard; and TAU, treatment as usual. T1 signifies 4 months after baseline; T2, 8 months after baseline; T3, 12 months after baseline (and treatment completion), and Treated, patients who had at least 1 postbaseline outpatient visit.

tives increases medication adherence,[9-13] and interventions that give relatives information about the illness and teach them coping and problem-solving skills reduce relapses and rehospitalizations.[14,15] McFarlane's Multi-Family Group (MFG) treatment is a behavioral family treatment that combines psychoeducation and skills training[16]; MFG has been shown to lower relapse rates, improve social functioning, and decrease caregiver burden relative to customary care.[17-21] Only 1 previous study[18] of MFG has demonstrated improved adherence in patients with schizophrenia.

Although MFG has features compatible with a cultural perspective,[22] we decided to test a cultural adaptation of the MFG that integrates throughout treatment the role of the sociocultural worlds of this largely immigrant Mexican-origin community. In contrast to past cultural adaptations that apply a more content-oriented treatment modification based on ethnic or linguistic categories (for a review, see Kopelowicz et al[14]), we took a more process-oriented approach to culture that recognizes the sociocultural context but at the individual patient or family level.[23] Accordingly, we modified MFG to target improved adherence using principles of the Theory of Planned Behavior, a well-researched social psychological theory[24] that has improved adherence to treatment in health-related interventions including treatment of coronary artery disease, hypertension, and human immunodeficiency virus infection.[25] This study evaluated the benefits of adding either our culturally modified MFG-adherence (MFG-A) or standard MFG (MFG-S) to treatment as usual (TAU) in a 3-arm, randomized clinical trial conducted at 2 community mental health centers (CMHCs) in the Los Angeles area that also included TAU alone. The participants were Spanish-speaking Mexican American patients with schizophrenia and a recent history of nonadherence to their antipsychotic medication regimens, and their key relatives.

METHODS

PARTICIPANTS

Patients were recruited from April 1, 2003, through January 31, 2007, from 6 inpatient psychiatry facilities (85%) and 2 outpatient CMHCs (15%) in the Los Angeles area. Patients were selected on the basis of the following criteria: (1) had diagnosis of schizophrenia or schizoaffective disorder, (2) was 18 to 50 years of age, (3) was of Mexican origin and spoke Spanish fluently (determined by self-report), (4) had been without antipsychotic medication without medical authorization for 1 continuous week in the month prior to study enrollment, (5) lived with their family of origin, and (6) had at least 1 family member willing to participate in the family treatment. In the inpatient units, individuals were contacted by a clinical staff member who discussed the study with them and alerted research staff if the individual expressed interest in participating. In the CMHCs, staff members identified patients who had a medical record diagnosis of schizophrenia or schizoaffective disorder and an exacerbation of psychotic symptoms within the previous month (as determined by the treating psychiatrist) and who were believed to be nonadherent to their antipsychotic medication regimens. Research staff contacted these individuals, provided information about the project, and conducted a structured interview and diagnostic assessment to verify that the individual met inclusion criteria. With the individual's permission, key relatives were contacted as soon as possible to assess their interest in participating.

As depicted in **Figure 1**, we recruited 178 dyads composed of a Spanish-speaking Mexican American with a *DSM-IV* diagnosis of schizophrenia or schizoaffective disorder and a key relative from 233 patients screened. Fourteen did not meet diagnostic criteria (ie, had diagnosis of psychotic disorder not otherwise specified or of substance-induced psychosis), and either the patient or key relative declined participation in the year-long intervention in 41 cases. Patients and families were encouraged to continue other psychosocial, psychopharmacologic, and educational interventions on their own during the study period. The last follow-up assessment was conducted in January 2009.

All participants had experienced a recent exacerbation of psychotic symptoms that was related to medication nonadherence. Medication nonadherence was operationalized as either the patient being without antipsychotic medication and medical authorization for 1 continuous week in the month prior to hospitalization, as documented in medical records, or the treating psychiatrist or family member reporting that failure to adhere to the medication regimen was a contributing factor to the recent psychotic exacerbation. Sample size was determined a priori on the basis of a power calculation that indicated a total of 180 participants would provide 80% power to detect a medium effect size if MFG-A was contrasted with the rest of the sample, including an adjustment for multiple comparisons.

After consent to participate was obtained, patients and their key relatives provided written consent using procedures approved by the institutional review boards of the David Geffen School of Medicine at UCLA and the Olive View/UCLA Medical Center (recruitment site for most patients who participated in this protocol). Patients were then randomized to 1 of the 3 study groups. Four patients dropped out before completing the baseline assessment, leaving 174 patients in the final sample. Patients were randomized to a study condition using a computer-generated random number table in cohorts of 5 to 8 patient–key relative dyads. Ten cohorts were assigned to the MFG-A group, 8 to MFG-S, and 9 to TAU, resulting in 64 participants in the MFG-A group, 53 participants in the MFG-S group, and 57 participants in the TAU group.

INTERVENTIONS

All study participants received TAU. To make the study as responsive as possible to the exigencies of clinical practice, rigid medication protocols were not used. Patients received all services as needed from the Mental Health Department of Los Angeles County. Those recruited as inpatients were assigned a case manager at the CMHC closest to their place of residence who scheduled an initial appointment with each individual to administer an "Adult Initial Assessment." The case manager designed a treatment plan, reviewed semiannually, for which he or she brokered services. Given caseloads of approximately 80 per case manager, the degree of monitoring varied, with the neediest receiving the most attention. Within a week of hospital discharge, patients were also scheduled for a psychiatric evaluation with a psychiatrist who performed a diagnostic and clinical assessment, prescribed medication, and, if the patient was clinically stable, scheduled monthly 20-minute sessions. If patients needed additional services, other members of the treatment team were enlisted. For example, if patients were in need of more extensive psychiatric rehabilitation, they were enrolled in a day treatment program at the centers for 40 hours per week, which included individual and group therapies. Finally, if patients experienced an exacerbation of symptoms, contact with the psychiatrist and/or psychiatric nurse increased (either at the clinic or in the field) until the patient was stabilized. For patients whose symptoms worsened too rapidly to be treated on an outpatient basis, arrangements were made for inpatient admission. These interventions are standard in all the CMHCs.

The MFG-S consisted of 3 components: (1) three initial "joining" sessions conducted separately with each family, (2) a 1-day (6-hour) multifamily "Survival Skills" educational workshop, and (3) multifamily group sessions as described by McFarlane.[16] The joining sessions were offered to each family (without the patient) to introduce the family to the therapist of the MFG sessions and to educate them about the need for ongoing treatment. The sessions also helped the family identify and overcome the obstacles to pursuing outpatient treatment. The Survival Skills Workshop[26] provided verbal and videotape information about the etiology, biology, genetics, symptoms, and treatment of schizophrenia. It was conducted in elementary school–level Spanish by 2 clinicians and one of us (A.K.). Following the workshop, each cohort began their MFG sessions twice monthly for 12 months (24 sessions total). All sessions were co-led by the 2 clinicians who conducted the 3 joining sessions and the Survival Skills workshop.

The first 3 sessions consisted of (1) introducing the participants to one another without a formal discussion of the illness, (2) discussing how schizophrenia had affected each of their lives, and (3) teaching problem-solving skills. Participants learned a 6-step problem-solving process[27]: define the problem, generate possible solutions, evaluate each, select one, implement it, and evaluate its outcomes. The subsequent 21 group sessions started with a brief "caring and sharing period" followed by group discussion. The discussion consisted of the sharing of personal experiences, the identification of a problem situation, and the use of the 6-step problem-solving method to address the situation within the context of general group support. The group ended with a review of the gains made by members that week. Members were free to select any problem, regardless of its relevance to medication adherence.

Culturally adapted, adherence-focused MFG (MFG-A) is based on 3 key constructs from the Theory of Planned Behavior posited to underlie taking (or not taking) action. *Attitudes* are beliefs and feelings about the consequences of the action. These beliefs may be factual or false, are held with varying degrees of certainty, and may be things we care about a great deal or very little. *Subjective norms* are our perceptions of the attitudes of significant others. Like our own attitudes, these may be true or false and their salience depends on the perceived importance of the other person. Finally, *perceived behavioral control* refers to whether we believe we have the necessary resources to act. Although the attitudes, subjective norms, and perceived behavioral control can be viewed as generic, individually based constructs, we argue that they oftentimes reflect culturally informed views associated with the local social worlds of the patients. We do not construe culture as tied solely to ethnicity, in this case of Mexican origin, but instead we view culture as related to many aspects of a person's local social world, including their socioeconomic status, religion, immigration status, and educational level.

In MFG-A, the joining sessions, the Survival Skills workshop, and the first 3 sessions were performed in the same manner as the MFG-S approach. After the session on problem-solving skills, the remaining 21 bimonthly MFG-A sessions differed from the MFG-S by focusing on specific obstacles to maintaining medication adherence guided by the Theory of Planned Behavior constructs. These obstacles were identified through individualized interviews with patients using the Theory for Planned Behavior Inventory (see Kopelowicz et al[28] for a complete description). The obstacles that the patients identified are embedded within their sociocultural context. For example, many indigent patients who did not have Medicaid believed they would be charged for their medication and therefore did not fill their prescriptions. Others believed that antipsychotic medication was necessary only for acute exacerbations of psychosis rather than for prevention of subsequent relapses. These patients often discontinued treatment soon after stabilizing, frequently leading to repeated hospitalizations.

In terms of changing *attitudes*, several sessions began by asking patients about their beliefs regarding the importance of taking medication. Patients often denied the value of medications, commonly expressing folk explanations (eg, supernatural causes) and corresponding remedies (eg, prayer) for psychotic symptoms.[29] The MFG-A clinicians sensitively addressed these attitudes by inviting relatives and other patients in the group, who initially may have held the same folk be-

liefs, to describe their salutary experiences with antipsychotic medications (eg, symptom reduction and preventing hospitalizations). This approach was instrumental in facilitating their consideration of alternative beliefs in a nonconfrontational, peer-to-peer manner.

A similarly structured intervention was implemented to alter *subjective norms*. Given the centrality of the family unit in decision making for Mexican Americans,[30] the focus was on the approval or disapproval of family members for taking medication and the patient's motivation to comply with those perceived wishes. The intervention was designed to correct patients' inaccurate beliefs about the opinions of others, and to change those opinions if they discouraged medication adherence.

Finally, the problem-solving activity in the MFG-A was particularly relevant in addressing *perceived behavioral control* because the Mexican American patients' relatives typically control resources, such as time and money needed to implement a solution.[31] Other families within the MFG often generated a wide range of solutions by recounting their successful and unsuccessful attempts to solve the same or similar problems. Control beliefs (what resources and opportunities the patient controls) and their perceived importance were elicited, and obvious inaccuracies were corrected by the group members and/or therapists.

GROUP FACILITATORS

All MFG sessions were led by bilingual and bicultural clinicians, including psychiatrists, psychologists, or social workers, with at least 1 year of experience conducting family groups. The clinicians were selected from the staff of the participating CMHCs on the basis of their stated interest in conducting family psychoeducational groups. These clinicians were trained during the start-up phase to competency by 2 of us (A.K. and R.Z.) according to the standard MFG treatment manual[16] and the MFG-A manual (available from the authors).

MISSED MFG SESSIONS

For both types of MFG, families were called before each session to remind them of upcoming sessions and, if necessary, to solve scheduling problems. Missed sessions occasioned a call from a research assistant to determine the reason (eg, forgetting, poor information, or conflicting life events). Concerns that raised group process issues or unwillingness to return to the group were referred to the MFG clinician and/or the case manager. Families and patients who stopped attending the groups were nevertheless encouraged to remain in treatment at the mental health center and to continue to provide research follow-up information throughout the study so that data analyses and research conclusions would be as complete as possible (as noted below, all analyses were based on all randomized cases). Treatment completion was defined as attending at least 75% of MFG sessions. Of the patients who attended at least 1 MFG session, 86% were classified as treatment completers.

MFG TREATMENT FIDELITY

Every MFG session was videotaped. Two of us (A.K. and R.Z.) reviewed all of the treatment videotapes and rated fidelity using the MFG Adherence and Competency Rating Scale (available from the first author [A.K.]). The scale included sections that assess adherence to specific MFG attributes, each rated on a 5-point Likert scale for presence/absence, protocol adherence, and competence. Two of us (A.K. and R.Z.) met monthly with the MFG clinicians to provide feedback. Overall, clinicians in both MFG conditions maintained high levels of fidelity ($\geq$4) to the treatment protocol.

ASSESSMENTS

Assessors were experienced study coordinators and bachelor-level research associates who completed a detailed training program before administering the clinical assessments. Training included didactic instruction followed by ratings of videotaped and live interviews following the protocol of the UCLA Research Center on Treatment and Rehabilitation of Psychosis. Upon completion of training, the assessors demonstrated interrater agreement on symptom ratings of $\kappa = 0.85$ and interrater agreement for the diagnoses of $\kappa = 0.94$. The assessors were unaware of the patient's and family's treatment condition and had no contact with either except for the actual occasion when ratings occurred.

INFORMANTS

Families each identified 1 key relative to serve as the primary informant for all assessments. In addition, the patient's treating psychiatrist and case worker were queried as needed, and the Los Angeles County Mental Health Department Management Information System (MIS) was used to collect information throughout the study.

ASSESSMENT SCHEDULE

Measures were gathered from patients and family members at baseline, at the end of the 12-month active treatment phase, and at the end of the 12-month follow-up period unless otherwise stated in the following description of each instrument. All measures were translated and adapted for use with the Spanish-speaking Mexican American group by one of us (A.K.). Participants were given $15 for each assessment.

INSTRUMENTS: PSYCHODIAGNOSTIC ASSESSMENT

Research diagnoses were obtained using the *Structured Clinical Interview for DSM-IV*.[32] All relevant sources of information were used to derive the diagnosis.

DEMOGRAPHICS AND CLINICAL HISTORY

The baseline research interview included the UCLA Aftercare Research Program's Client Data Inventory, a comprehensive assessment designed to elicit demographic information and clinical history variables.

ADHERENCE TO MEDICATION

Adherence was coded at baseline, every 4 months in the first year, and every 6 months in the second year. Data were gathered by a research associate who was masked to treatment condition at each scheduled or nonscheduled psychiatric visit (but at least every 4 months) for a maximum of 2 years (12-month outpatient intervention plus 12-month follow-up). For patients recruited from the outpatient settings, data collection began on the day the informed consent process was completed; for those recruited from the inpatient units, data collection started on the first day following discharge from the inpatient ward.

The research associate interviewed patients using the patient section of the Treatment Compliance Interview.[33] This instrument provides a quantified rating of the extent to which the patient did or did not take the target medication during the past month and the amount of medication he or she may have taken. The patient's designated key relative was also inter-

viewed using the relative version of the Treatment Compliance Interview. In addition, the key relative was trained to observe unobtrusively and to update an ongoing record of the same variables that appeared on the patient's self-assessment rating sheet. The patient's psychiatrist was queried on a monthly basis and asked to rate the likelihood of medication compliance (0 = not compliant at all, 5 = always compliant). Pharmacy data from the Los Angeles County MIS were also accessed to determine whether patients obtained their antipsychotic medication. Pharmacy data were available for all patients in the intention-to-treat sample, and thus adherence could be assessed even for patients who discontinued treatment at the CMHC (ie, failure to fill any prescriptions after dropout would be rated as not compliant at all). Discrepancies between the different sources of information were resolved by investigator consensus.

Consistent with previous work,[33] the data on medication adherence were scored for amount (complete vs partial vs none) and time (continuous vs transient vs nonadherent). The percentage of times the patient took the prescribed medication at the prescribed time (continuous measure) was determined. Failure to take any antipsychotic medication for 14 consecutive days in each assessment period was used to differentiate continuous vs transient nonadherence. Adherence was then categorized on an ordinal scale derived from the Treatment Compliance Interview using the following designations: nonadherent (<50% adherent), partially adherent (50%-80% adherent), and adherent (>80%).

HOSPITALIZATIONS

The MIS was used to collect information on use of inpatient resources. The MIS tracks the use of all mental health services provided by both public (indigent) and private (Medicaid) providers within Los Angeles County. The MIS was queried for each patient every 4 months during the first year of study participation and every 6 months for the second year.

SYMPTOM ASSESSMENT

Psychiatric symptoms were assessed using the Brief Psychiatric Rating Scale (BPRS).[34,35] This semistructured instrument is based on patient self-report and clinician observation of the patient's behavior and speech. Signs and symptoms are rated along a severity and impairment-in-functioning dimension using a 7-point rating scale. The reliability of the 2 BPRS raters was assessed with a subgroup of patients at baseline (n = 26, interclass correlation coefficient = 0.87) and at the quality assurance check 6 months after baseline (n = 24; interclass correlation coefficient = 0.82). A total BPRS score and a BPRS psychosis factor that included suspiciousness, hallucinations, unusual thought content, and conceptual disorganization were used in the data analysis.

STATISTICAL ANALYSIS

Data were analyzed using SAS statistical software, version 9.1.3 (SAS Institute, Inc, Cary, North Carolina). Demographic and descriptive characteristics were summarized and compared using χ^2 tests and analyses of variance as appropriate, using $\alpha = .05$ for individual level of significance. For all analyses, we followed the intent-to-treat principle, analyzing data for all randomly assigned participants according to the experimental arm to which they were assigned.

Analysis of adherence used a dichotomous recoding (complete vs partial or none) because the numbers in the partial category became small over time (all cells fewer than n = 10). A logistic regression model with repeated measures was fit using SAS GLIMMIX on follow-up data at 4, 8, 12, 18, and 24 months, specifying an unstructured covariance matrix for the repeated measures based on likelihood criteria (Akaike Information Criterion and corrected Akaike Information Criterion). We examined the fixed effects for time, intervention condition, and their interaction. A multinomial regression (SAS GENMOD) using the 3 categories (none, partial, and full) yielded similar results and is not reported.

Hospitalization data were coded during the same 5 intervals (1-4, 5-8, 9-12, 13-18, and 19-24 months after baseline), but the primary analysis used the life-table method of survival analysis (SAS LIFETEST) on an overall measure (ever hospitalized), stratifying by treatment group and using the log-rank test for tests of group differences. Path analysis was used to explore the hypothesis that adherence plays a mediating role accounting for the effect of treatment on hospitalization.[36,37] The mediating hypothesis was that adherence would predict hospitalization even if treatment was in the model, and that the direct effect of treatment would be attenuated or eliminated when adherence was included. The primary analysis used variables summarizing adherence and hospitalizations across the entire follow-up period (more complex models not reported that used repeated measures after baseline yielded substantively equivalent results). The mediation path is the multiplicative one that combines the effect of treatment on adherence and then of adherence on hospitalization, controlling for treatment. The measure of hospitalization for this analysis was a dichotomy defined as any hospitalization during follow-up. The measure of adherence was a dimensional measure obtained by summing the repeated dichotomous measures of adherence after baseline, yielding a summary score from zero (never adherent) to 5 (adherent at all postbaseline visits). On the basis of the other outcome analyses previously described, the treatment variable was coded as a dichotomy contrasting MFG-A with the other 2 groups (see the "Results" section). Regression and multiple regression analyses were performed to estimate the regression paths and the standard errors, and the Sobel test[38] was used to determine significance.

The effect of treatment on BPRS symptom severity ratings and the BPRS psychosis factor were analyzed separately with a mixed-effects regression analysis (baseline, 12-month, and 24-month assessments) using an unstructured covariance matrix to accommodate unequal BPRS variances at baseline and thereafter (analysis of covariance on the postbaseline scores controlling for baseline yielded essentially equivalent between-group results as the repeated-measures analysis). Because there was differential dropout in the treatment groups, we also analyzed the data using inverse propensity scores derived from baseline data as case weights.

RESULTS

DEMOGRAPHIC AND CLINICAL CHARACTERISTICS

The demographic and clinical characteristics of the 174 randomized patients at enrollment are presented in the **Table**. This list includes the last antipsychotic medication prescribed to the patient before study enrollment. No significant differences between groups were found on baseline variables.

MEDICATION ADHERENCE

Results are depicted in **Figure 2**. Across the 24 months of the study (12 months of treatment and 12 months of

Table. Baseline Characteristics of the Intention-to-Treat Cohort[a]

Characteristic	MFG-A (n=64)	MFG-S (n=53)	TAU (n=57)
Male sex, %	67	68	61
Single marital status, %	78	77	63
Employed, %	16	11	21
Age, mean (SD), y	32.6 (11.3)	29.6 (10.8)	32.8 (12.6)
Age at onset, mean (SD), y	24.6 (8.3)	22.7 (7.6)	22.5 (9.2)
Educational level, mean (SD), y	8.8 (3.5)	9.7 (2.6)	9.8 (2.9)
Lifetime hospitalizations, mean (SD)	5.5 (5.2)	5.6 (6.3)	7.1 (6.3)
Inpatient at entry, No. (%)	56 (88)	44 (83)	48 (84)
BPRS total score, mean (SD)	87.5 (5.8)	85.8 (6.8)	81.1 (6.3)
BPRS psychosis, mean (SD)	21.0 (3.0)	19.9 (2.9)	19.7 (3.1)
Antipsychotic type, No. (%)			
1st-generation oral	44 (69)	34 (64)	36 (63)
2nd-generation oral	10 (16)	8 (15)	11 (19)
Long-acting injection	2 (3)	1 (2)	1 (2)
None	8 (13)	10 (19)	9 (16)

Abbreviations: BPRS, Brief Psychiatric Rating Scale; MFG-A, multifamily group-adherence; MFG-S, multifamily group-standard; TAU, treatment as usual.
[a] All group differences are nonsignificant.

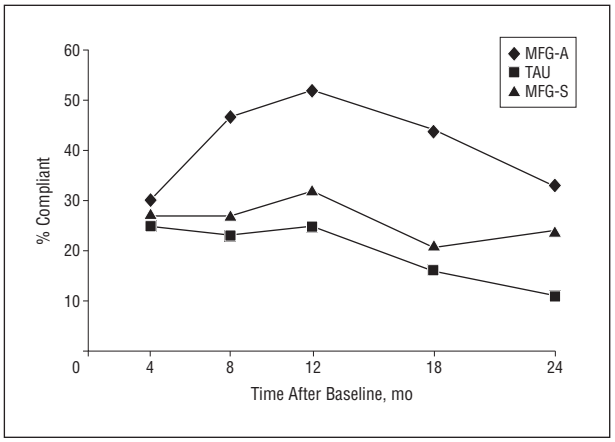

Figure 2. Adherence to medication by group in the intention-to-treat sample. MFG-A indicates multifamily group-adherence; MFG-S, multifamily group-standard; and TAU, treatment as usual.

follow-up), there were significant main effects of treatment on adherence for group ($F_{2,172}$=6.41, P=.003) and for time ($F_{4,172}$=3.5, P=.009), but not the group × time interaction ($F_{8,171}$=1.4, P=.22). More participants in MFG-A were fully adherent than those in TAU at all assessments after 4 months (all $P < .01$), and MFG-A was significantly better than MFG-S at 8 (P=.03), 12 (P=.04), and 18 months (P=.01), but not at 24 months (P=.20). There was no significant difference at any point between the MFG-S and TAU groups.

HOSPITALIZATION

As shown in **Figure 3**, the overall test for group differences in time to first hospitalization after baseline was significant (log-rank χ^2_2=13.3, P=.001). Follow-up comparisons using proportional hazard regression indicated that MFG-A participants had longer time to first hospitalization than MFG-S (χ^2_1=6.3, P=.01) and TAU (χ^2_1=8.7,

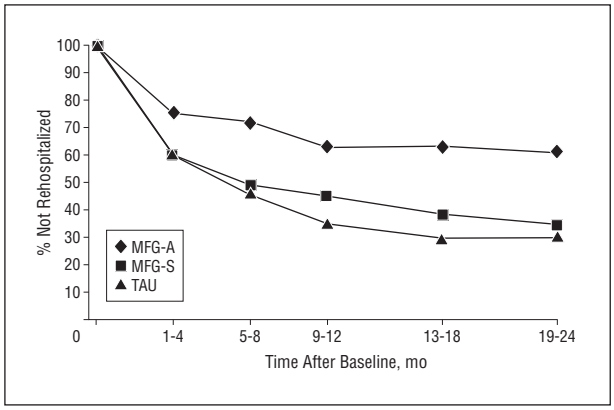

Figure 3. Time to hospitalization by group in the intention-to-treat sample. MFG-A indicates multifamily group-adherence; MFG-S, multifamily group-standard; and TAU, treatment as usual.

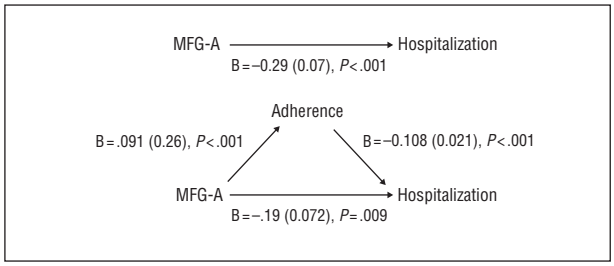

Figure 4. Mediation analysis of treatment effect on adherence and hospitalization. MFG-A indicates multifamily group-adherence. N=174. Sobel: 2.92, P=.004 (34% of the MFG-A–hospitalization association).

P=.003). Across the entire follow-up period, hospitalization was less likely for those in MFG-A (39%) than for those in MFG-S (66%, χ^2_1=8.2, P=.004) or TAU (70.2%, χ^2_1=11.3, $P<.001$). The latter groups did not differ (χ^2_1=0.2, P=.64).

MEDIATION ANALYSIS

As seen in **Figure 4**, the single regression path from treatment (MFG-A vs others) to hospitalization (any vs none) was highly significant (B=–0.29, SE=0.07, t=–3.88, $P<.001$). The first part of the mediation path is the MFG-A effect of adherence, summarized in this analysis by a single regression coefficient based on the overall adherence measure (B=0.91, SE=0.26, t=3.53, $P<.001$). The second part is the effect of adherence on hospitalization when MFG-A is included in the multiple regression model (B=–0.108, SE=0.021, t=–5.18, $P<.001$). The mediating path from treatment (MFG-A) through adherence to hospitalization is the product of these regression coefficients. It is highly significant (Sobel test=2.92, SE=0.033, P=.004). Increased adherence associated with MFG-A accounted for approximately one-third of the overall effect of MFG-A on reduced risk of hospitalization.[39] In addition, there was a significant path from MFG-A to hospitalization reduction even after adherence was included in the model (B=–0.19, SE=0.072, t=–2.4, P=.009).

VERY EARLY DROPOUT AND ATTRITION

A substantial proportion of patients (45 of 174 [26%]) dropped out of treatment immediately after undergoing

baseline assessments and before engaging in ongoing outpatient care. There were no statistically significant differences at baseline between these "baseline-only" patients (n=45) and those patients who had at least 1 outpatient treatment visit (n=129) on any demographic or clinical variable except for mean (SD) total BPRS score (baseline only: 89.0 [12.5]; all others: 83.1 [21.0]; $t=2.23$; $P=.03$). Baseline-only patients were less likely to be medication adherent ($P=.002$) and more likely to be hospitalized ($\chi^2=8.2$, $P=.004$) than TAU patients who had at least 1 postbaseline treatment visit. However, a comparison of the 3 treatment groups excluding the baseline-only patients found essentially the same results as with the full sample on these 2 variables.

There was a significant difference in attrition, defined as leaving treatment before a posttreatment (12-month) assessment could be attained (logistic regression score: $\chi^2_2=7.7$, $P=.02$). The MFG-A participants (27%) were less likely to drop out of treatment than TAU participants (51%, $\chi^2_1=7.4$, $P=.007$), but MFG-S participants (37%) were not different from MFG-A ($\chi^2_1=1.2$, $P=.28$) or TAU ($\chi^2_1=2.5$, $P=.11$). This is important for the outcome analyses because dropouts were less adherent ($t_{172}=8.9$, $P<.001$; unequal variances $t_{166.11}=10.42$, $P<.001$) and more likely to be hospitalized during follow-up ($\chi^2_1=5.9$, $P=.02$).

BRIEF PSYCHIATRIC RATING SCALE

Results of weighted and unweighted analyses were not substantively different so we report the results of the unweighted analyses. There were no differences at baseline on the mean BPRS scores among the 3 treatment groups ($F_{2,171}=1.76$, $P=.18$). The repeated-measures analysis of variance yielded only a significant time effect ($F_{2,171}=90.3$, $P<.001$). At the end of treatment (12 months after baseline), all 3 groups improved significantly on the BPRS relative to baseline (time $F_{1,171}=154.5$, $P<.001$), but there was no group × time difference ($F_{2,171}=1.14$, $P=.32$). There was no significant change in BPRS scores between the end of treatment and the 24-month follow-up in any of the 3 treatment groups (range of *P* values: .30-.60). Separate analyses of the BPRS psychosis factor yielded essentially equivalent results.

COMMENT

This study evaluated the efficacy of culturally adapted MFG therapy to enhance adherence for Spanish-speaking patients with schizophrenia and a recent history of nonadherence to antipsychotic medication. During a 2-year follow-up period, MFG-A was associated with greater medication adherence and more positive clinical outcomes compared with MFG-S and TAU. We found that medication adherence accounted for a significant proportion of the variability in positive outcomes, and for approximately one-third of the treatment effect on hospitalization. This clinical trial was performed with a hard-to-reach community of Spanish-speaking Mexican Americans. It thus extends the efficacy of MFG treatment, particularly the adapted form, for other culturally diverse patients and their families.

MFG DIRECTED AT IMPROVING ADHERENCE

Given that adherence is a central issue in the delivery of effective treatment of schizophrenia, the findings that MFG-A outperformed the other 2 conditions demonstrates the value of this approach. The improvement observed in the MFG-A group was clinically meaningful. The MFG-A participants were twice as likely as comparison patients to be medication adherent at the end of the 1-year treatment and only half as likely to be hospitalized during the 2-year follow-up. Furthermore, the reduction in psychiatric hospitalization in the MFG-A participants was partially mediated by increased adherence to antipsychotic medication. This study points out the value of addressing adherence within the context of family treatment but also suggests that other salutary aspects of MFG (eg, active engagement of patients and families in treatment, communication skills training, problem-solving approach, and social network development) may have contributed to decreased attrition and reduction in hospitalizations.[16]

CULTURALLY ADAPTED MFG TREATMENT FOR SPANISH-SPEAKING MEXICAN AMERICANS

Our results demonstrate that the cultural adaptation of MFG to focus on adherence can be applied successfully to Spanish-speaking Mexican American families and their ill relatives who are nonadherent. Treatment adherence is embedded in a rich sociocultural network of beliefs, attitudes, and social norms as well as available social resources. The clinicians' systematic assessment of the beliefs, attitudes, and resources of each patient, and the integration of those factors in treatment, played a central role in the success of the MFG-A. For example, many of the patients who did not have or were ineligible for medical benefits did not take their medications because they could not afford to purchase them. These patients and their families did not realize they could receive antipsychotic medications at no cost through an indigent medication program available at the mental health center. After identifying the perceived lack of resources, the MFG-A clinicians used the problem-solving method and drew on the group's sociocultural resources to design a culturally informed action plan that overcame this obstacle to medication adherence. Our cultural adaptation emphasizes a process that assesses the specific attitudes and beliefs of the individual patient and draws on the social norms and sociocultural resources of the group to help patients in achieving their goals. By giving a voice to the patients and their families at multiple junctures, we were able to assist patients to become adherent in ways that not only respected but integrated the rich social fabric of their everyday lives. The strength of this process-oriented cultural adaptation is that it does not make assumptions about the given attitudes and social norms of the patient given their ethnicity or race.

The lack of difference between standard MFG and TAU on medication adherence was somewhat surprising given the results of several long-term studies[16,40] of standard MFG demonstrating benefits during a 5-year follow-up period. One explanation for the results of this study is

that the current sample consisted exclusively of patients who were nonadherent to their medication regimens. To our knowledge, no previous study of MFG had focused on this population. It should be noted that MFG-A failed to maintain its statistical superiority compared with MFG-S beyond the 18-month assessment point. Inspection of Figure 2 suggests that this finding may have resulted from the decreased adherence of the MFG-A group at 24 months compared with previous assessment periods. This relative loss of efficacy over time indicates the possible need for booster sessions to sustain the benefits of the intervention.

Mean scores on the BPRS for the 3 treatment conditions decreased significantly (ie, from the mid-80s at baseline to the mid-50s at the 12- and 24-month assessments), with minimal differences between the 3 groups. Given the overall increase in medication adherence and decrease in psychiatric hospitalizations of patients in the MFG-A condition, the lack of significant group differences in the analysis of psychotic symptoms at the 12- and 24-month assessment points was unexpected. A plausible explanation is that the BPRS data were not obtained from dropouts, whereas medication adherence and hospitalization data were available for all patients through the Los Angeles County Department of Mental Health's MIS. Patients who dropped out of treatment were more likely to be nonadherent to their medication regimens, more likely to be hospitalized, and less likely to be in the MFG-A group.

Several limitations in evaluating the results of this study should be recognized. First, although the evaluation of adherence incorporated multiple sources, no objective measure of adherence (eg, antipsychotic blood level or electronic bottle cap) was used. Second, the inclusion criteria required that all participants live with their families of origin, which may restrict the applicability of the findings to those patients who remain in contact with family. Third, categories were collapsed (eg, partial and no adherence; MFG-S and TAU) because of limited power for some analyses. Fourth, 26% of the study patients (most of whom were recruited while inpatients) dropped out of treatment immediately after undergoing the baseline assessments and before engaging in ongoing outpatient care. The TAU patients (37%) were more likely than MFG patients (21%) to drop out before engaging in outpatient treatment, thus providing further evidence for the value of family groups.

Given that Mexican Americans are among the ethnic groups least likely to receive quality mental health care,[41] and that Spanish-speaking individuals with schizophrenia receive fewer mental health services than English-speaking people with schizophrenia,[42] our findings contribute to the study of disparities in mental health care for Latinos. Steps can be taken to improve the generally poor quality of mental health care for Spanish-speaking persons. Although there are a number of studies that indicate services can be improved for Latinos with depression,[43,44] this is among the few rigorous clinical treatment studies focusing on Spanish-speaking individuals with a psychotic disorder.[14,45] Clinicians working with this population might incorporate a culturally adapted, adherence-focused MFG treatment to improve the course and outcome of schizophrenia as a component of clinical care. Moreover, given the individualized process orientation of our cultural adaptation, it may prove useful in psychosocial interventions for schizophrenia-spectrum disorders applied to communities from a wide range of sociocultural backgrounds.

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