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Impact of a Mobile Health Intervention on Long-term Nonadherence After Lung Transplantation: Follow-up After a Randomized Controlled Trial

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Abstract

Background.—In a randomized controlled trial, lung transplant recipients (LTRs) using a mobile health intervention, Pocket Personal Assistant for Tracking Health (Pocket PATH), showed better adherence to the medical regimen than LTRs receiving usual care during the first year posttransplant. We examined whether these effects were maintained beyond the end of the trial and evaluated other potential risk factors for long-term nonadherence.

Methods.—Adherence in 8 areas was evaluated at follow-up in separate LTR and family caregiver (collateral) assessments. Pocket PATH and usual care groups' nonadherence rates were

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compared; multivariable regression analyses then examined and controlled for other patient characteristics' associations with nonadherence.

Results.—One hundred five LTRs (75% of survivors) were assessed (M = 3.9 years post-transplant, SD = 0.8). Nonadherence rates in the past month were 23%–81% for self-care and lifestyle requirements (diet, exercise, blood pressure monitoring, spirometry), 13%–23% for immunosuppressants and other medications, and 4% for tobacco use, with 31% clinic appointment nonadherence in the past year. In multivariable analysis, the Pocket PATH group showed lower risk of nonadherence to lifestyle requirements (diet/exercise) than the usual care group ($P < 0.05$). Younger age and factors during the first year posttransplant (acute graft rejection, chronically elevated anxiety, less time rehospitalized, nonadherence at the final randomized controlled trial assessment) were each associated with nonadherence in at least 1 area at follow-up ($P < 0.05$).

Conclusions.—Pocket PATH did not have sustained impact on most areas of the regimen, although we identified other risk factors for long-term nonadherence. Future work should explore strategies to facilitate sustained effects of mobile health interventions.

INTRODUCTION

Mobile health (mHealth) refers to the use of mobile wire-less devices to support health care and public health,[1,2] and mHealth technologies offer promising solutions for the challenge of nonadherence in lung transplant recipients (LTRs). Nonadherence to the multicomponent posttransplant regimen is prevalent in LTRs, with rates as high as 70% for some elements of the regimen by 2–3 years post-transplant.[3–7] Clinical outcomes can suffer as a result.[6–9] Many tasks comprising the regimen (eg, taking immunosuppressants, monitoring lung function) are amenable to the algorithmic assistance offered by mHealth. Moreover, transplant recipients have favorable attitudes toward use of mHealth for this purpose,[10–13] and there have been calls for evidence-based mHealth interventions to address adherence issues in transplantation.[14–16]

mHealth interventions have included internet strategies, software on tablet computers, wearable behavior monitoring devices, and smartphone applications (apps).[1,2,14,16] One such intervention—the Pocket Personal Assistant for Tracking Health (Pocket PATH)—is a smartphone app designed to enhance performance of all aspects of the post lung transplant regimen.[17] Unlike most apps which reach consumers with little to no empirical evaluation, [18–22] Pocket PATH is one of a limited number of mHealth interventions[2,19,21–23] to have undergone user-centered development and testing.[17,19,24,25] Moreover, it focuses specifically on transplant recipients and, beyond several pilot studies,[26,27] Pocket PATH remains the only such app in transplantation evaluated in a full-scale randomized controlled trial (RCT) (NCT00818025).[17] Its features include alerts and reminders about medication-taking and other behaviors, options to track health indicators and symptoms, and decision support tools guiding patients on when to seek transplant team assistance. In an RCT with 201 LTRs followed through the first year posttransplant, those receiving Pocket PATH showed better medical regimen adherence than patients receiving usual care.[17]

However, little is known about whether any mHealth intervention targeting nonadherence, including Pocket PATH, has sustained effects beyond the relatively brief periods of use in

research investigations.[14,23,28–30] This gap precludes understanding of the full value of mHealth strategies,[14] especially in light of average longevity in patients after transplantation.[14] In addition, the lack of information on long-term, sustained impact is of particular concern because self-motivated adherence to the regimen becomes increasingly important as the time since transplant grows longer, clinical follow-up becomes less frequent, and recipients assume greater responsibility for monitoring their health. Identifying predictors of non-adherence well beyond the early years posttransplant is therefore also important but has proved challenging. Even early posttransplant, existing evidence on putative risk factors is mixed and inconsistent.[4,5,7,31–34]

To assess whether Pocket PATH had sustained effects on LTRs' medical regimen adherence beyond the 1-year period of the original RCT, we conducted a long-term follow-up study of trial participants. They averaged ~4 years posttransplant at follow-up. Our primary goal was to determine whether assignment to the Pocket PATH intervention reduced long-term nonadherence to the medical regimen, relative to usual care. Our secondary goals were to (a) describe long-term nonadherence in this population, for which there are few data beyond 2–3 years posttransplant, and (b) identify patient characteristics that increase risk for long-term nonadherence.

MATERIALS AND METHODS

Study Participants

Participants were enrolled in the original RCT[17] in January, 2009 through December, 2011 during hospitalization for lung transplantation at the University of Pittsburgh Medical Center. The RCT followed them during the first year post-transplant. Eligible LTRs were first-time transplant recipients ≥18 years of age who read and spoke English; 75% of eligible patients were enrolled.[17] We recontacted participants for follow-up in March through September, 2014.

Procedure

The University of Pittsburgh Institutional Review Board approved the original and follow-up studies. LTRs provided written informed consent in the original trial, and electronic or verbal consent for the follow-up assessment.

The original RCT's procedures have been described.[17] In brief, LTRs were randomized to the Pocket PATH intervention or usual care study arms before hospital discharge posttransplant. Patients in both groups received identical discharge instructions regarding self-management. During the RCT, their adherence to the posttransplant medical regimen was assessed during the first year at 2, 6, and 12 months, as described below.

LTRs in the intervention group received a smartphone with the Pocket PATH app with features allowing them to set reminders for medication-taking and appointments, and record and view graphs for the health indicators that the transplant program required them to monitor. If health indicator values fell beyond preestablished ranges, Pocket PATH provided decision-support messages instructing them to contact their transplant coordinator.

LTRs in the usual care group received the transplant program's standard paper-and-pencil tracking logbook in which they were to record values for the health indicators they were required to self-monitor. If LTRs determined these values met criteria as abnormal, they were to contact their transplant coordinator.

At the RCT's conclusion, LTRs in the Pocket PATH group kept the smartphone and could have continued to use the app. However, the app's automatic decision-support feature no longer functioned for any participant because the phone's data plan ended. LTRs were not prospectively followed to determine whether and for how long they continued to use the app.

For the follow-up study, we recontacted LTRs to assess medical regimen adherence and psychosocial status (including whether LTRs assigned to Pocket PATH were still using it). Depending on their preference, they were assessed by telephone (by a trained interviewer) or via a secure internet-based form (Qualtrics, LLC); there were no significant differences due to assessment mode for any variable. We also contacted each LTR's primary family caregiver (the person they identified as providing them the most care and assistance). After providing informed consent, the caregiver completed an assessment of the LTR's adherence at follow-up.

Measures

Nonadherence at Long-term Follow-up—Self-report (alone or combined with other methods such as collateral report) identifies nonadherence rates as high or higher than any other method[7,35–37]; a multimethod approach is recommended.[38] Thus, at follow-up (and in the original RCT), we assessed nonadherence using a combination of patient and family caregiver report.

Specifically, we used the Health Habits Survey,[39,40] a reliable, validated instrument used in various transplant populations.[4,40,41] It assesses frequency of performing elements of the posttransplant regimen during the prior month, the recommended timeframe for maximizing accurate recall.[37] We assessed nonadherence in 8 areas: (a) taking the primary immunosuppressant, (b) taking other medications, (c) attending clinic appointments, (d) performing home spirometry, (e) monitoring blood pressure, (f) following a prescribed diet, (g) following a prescribed exercise plan, and (h) abstaining from tobacco use. (Clinic appointment attendance was assessed over the past y rather than the past mo because LTRs were not required to have monthly visits.) Although questions used an ordinal response format to indicate activity frequency, we dichotomized responses to indicate whether LTRs met the minimum level of adherence acceptable to the transplant program (eg, missing the primary immunosuppressant less than once monthly; see Results section).

As in the original RCT, because we employed both patient and collateral reports, we created a single measure of non-adherence for each of the 8 areas by taking any report of nonadherence, whether from patient or caregiver, to indicate nonadherence. We created an overall measure of nonadherence by summing the number of areas to which LTRs were nonadherent. Although all LTRs had family caregivers who could serve as collaterals in the original RCT (because having a caregiver was required for transplant), 24% of patients reported they no longer had a caregiver at follow-up. For such patients, adherence was based

on their own report. Nonadherence rates did not differ between these patients and the remainder of the cohort (see Results section).

Potential Predictors and Correlates of Long-term Nonadherence—Our primary predictor was whether participants were in the original Pocket PATH intervention versus usual care groups (Table 1). We examined additional potential predictors and correlates at follow-up based on the World Health Organization's model of nonadherence[42] and evidence from adherence research in cardiothoracic transplant populations.[3,5,6,31–34] Thus, at original RCT enrollment, we collected information on sociodemographics, psychosocial characteristics, and transplant-related medical factors.[43–50] We also collected information on health- and adherence-related characteristics during the period of the original trial (first year posttransplant), and psychosocial and health-related characteristics beyond the end of the original trial through the time of follow-up.[51–53]

Statistical Analysis

We compared the 2 study groups on all characteristics using *t* tests and χ^2 tests (or Fisher exact test when necessary). We used *t* tests, χ^2 tests, and McNemar tests to examine whether the entire cohort's nonadherence rate in each area of the regimen changed from the end of the RCT to the follow-up assessment and whether nonadherence in each area at the end of the RCT was associated with non-adherence at follow-up (ie, whether LTRs nonadherent at the RCT's end were likely to be the same LTRs nonadherent at follow-up).

To identify predictors and correlates of nonadherence at follow-up, we used linear regression (for total number of areas of nonadherence) and logistic regression (for each individual area of the regimen). A separate model was fit for each outcome. Variables were entered into the model in 3 sequential stages to reflect their temporal ordering.[54] First, baseline variables assessed at RCT enrollment were entered to examine their effects. Then, variables related to patients' status during the first year posttransplant (the period of the RCT) were added to determine their contributions beyond the baseline characteristics. Finally, variables related to the follow-up period were added. Two variables were forced into the modeling: (a) RCT study arm (Pocket PATH versus usual care) because it was a study design characteristic and (b) whether patients were nonadherent at the end of the original RCT in the area of the regimen under consideration as the outcome at follow-up (eg, if the outcome was medication-taking, we examined past nonadherence to medication-taking). We ensured that regression analytic assumptions were met and that our final models maintained a participant-to-variable ratio within the recommendations of 10:1.[54]

RESULTS

Participant Characteristics

Of 201 recipients in the original RCT, 19 were deceased before the end of the trial and 42 deaths occurred before our follow-up. Of the 140 recipients alive at follow-up, 12 (9%) could not be contacted. Of those contacted, 20 (16%) refused and 3 (2%) were too ill to participate. Thus, 105 were enrolled, yielding a response rate of 75% of surviving patients and 82% of those who could be contacted. The 105 participants did not significantly differ

from the 35 surviving nonparticipants on characteristics assessed in the original RCT, or on subsequent rates of acute rejection or BOS (Table S1, SDC, http://links.lww.com/TP/B775).

At contact, the 105 participants were an average of 3.9 years posttransplant (SD = 0.8, median = 3.9, IQR = 3.3–4.4, range 2.4–5.7). Table 2 provides descriptive information, and shows that the Pocket PATH and usual care groups were similar on most measures. The only significant differences were that LTRs assigned to Pocket PATH had a shorter hospital stay posttransplant and were less likely to have a family caregiver at follow-up. Only 2 LTRs were using Pocket PATH at follow-up, and thus this characteristic could not be considered further.

Finally, with respect to nonadherence by the end of the original RCT, the first set of 4 columns of Table 3 shows that, consistent with findings for the full cohort in the original trial,[15] the Pocket PATH group had a significantly lower total number of nonadherent areas, on average, than the usual care group. The largest contributors to this difference were lower nonadherence to blood pressure monitoring and, to a lesser extent, lower nonadherence to spirometry in the Pocket PATH group (Table 3).

Nonadherence Rates at Long-term Follow-up and Comparison to Rates at End of RCT

The second set of 4 columns in Table 3 shows nonadherence rates for all 105 study participants at the follow-up, and rates separately by study group. There were no significant differences between Pocket PATH and usual care groups for total number of areas of nonadherence or any single area of the regimen.

Comparing the cohort of 105 participants at the follow-up versus the end of the RCT, Table 3 shows that nonadherence rates were higher at follow-up in all areas. This overall difference was statistically significant for the total number of nonadherent areas and, specifically, for nonadherence to clinic appointments, spirometry, and exercise requirements (Table 3, next to last column). We also examined whether LTRs nonadherent in a given area at follow-up were the same LTRs nonadherent in that area at the end of the RCT (ie, whether later nonadherence was associated with earlier nonadherence). The last column of Table 3 indicates that in 5 of the 8 areas (as well as total number of areas nonadherent), there was a statistically significant association.

Potential Risk Factors and Correlates of Long-term Nonadherence

To reduce type I error risk, we took steps to limit the number of tests examining variables' associations with nonadherence outcomes. First, we reduced the number of outcomes by (a) creating a measure of medical non-adherence by grouping the primary immunosuppressant and other medications measures, (b) creating a measure of nonadherence to lifestyle requirements by grouping nonadherence to either diet or exercise requirements, and (c) eliminating tobacco use from consideration because it occurred too infrequently. Second, before multivariable analyses, we examined bivariate associations of each potential risk factor or correlate with the nonadherence outcomes. Although intervention group and nonadherence at the end of the original RCT were included in all regression models (see Methods), other potential risk factors or correlates that showed small associations ($r \leq 0.15$)

with all nonadherence domains were excluded from multivariable analyses (see Table 4, footnote *a*).

Remaining factors were included in the regression analyses; results are in Table 4. For total number of areas for which LTRs were nonadherent, the table presents unstandardized regression coefficients from linear regression and 95% confidence intervals. For dichotomous nonadherence outcomes, the table presents odds ratios generated from the logistic regression coefficients and 95% confidence intervals.

Among baseline characteristics (first 3 rows of Table 4), younger age increased patients' risk of nonadherence to blood pressure monitoring at follow-up. Among factors reflecting the status of the patients during the original RCT, the Pocket PATH group had a lower risk of non-adherence to lifestyle (diet/exercise) requirements. Longer total rehospitalization time during the first year posttransplant reduced patients' risk of nonadherence to blood pressure monitoring. Patients with more rejection episodes in the first year posttransplant had a greater total number of nonadherent areas at follow-up and, more specifically, were more likely to be nonadherent to medications, spirometry, and blood pressure monitoring. Patients with elevated anxiety at a greater number of assessments during the first year posttransplant had a greater total number of nonadherent areas at follow-up and were more likely to be nonadherent to medications. Nonadherence at the end of the original RCT predicted nonadherence in only 1 area, diet/exercise requirements. Finally, clinically significant psychological distress at follow-up was not associated with any nonadherence outcome.

DISCUSSION

Our study is one of the first to evaluate the long-term efficacy of an mHealth intervention in promoting adherence to the medical regimen after organ transplantation. Although the Pocket PATH intervention led to less non-adherence during the first year after lung transplantation relative to usual care,[17] our follow-up of LTRs at an average of 4 years posttransplant indicated that Pocket PATH's short-term adherence benefits were generally not sustained. Specifically, after controlling for other nonadherence risk factors, patients assigned to Pocket PATH in the original RCT were less likely to show lifestyle (diet/exercise) non-adherence at follow-up, but there was no evidence of intervention impact on other nonadherence outcomes.

These findings may be due in part to the fact that all but 2 LTRs discontinued Pocket PATH use by the time of follow-up. Although we did not systematically query LTRs about reasons for discontinuation or other barriers to sustained use, the discontinuations are consistent with steep declines in patient engagement observed with other mHealth technologies,[14,55] and, indeed, with other types of adherence-promoting interventions.[56,57] For mHealth technologies in particular, patients may discontinue use because they do not feel they are effective or because they no longer meet patients' changing needs. For example, anecdotal patient remarks suggested that, at follow-up, they perceived less value in performing spirometry and blood pressure monitoring (the areas with the highest nonadherence rates) in the long-term compared with perceived value in the first year posttransplant (when these 2 areas showed the largest impact of Pocket PATH over usual care; see Table 3).

Even if discontinued, early use of mHealth technologies, including Pocket PATH, may facilitate habit development that may not require continued intervention to be sustained.[12] Although this might be suggested by our finding that the Pocket PATH group was less nonadherent to lifestyle requirements (diet/exercise) at follow-up, our findings are largely inconsistent with such an explanation, given that there were no other adherence differences between study groups.

In fact, the notion of "habit formation" is likely too simplistic when applied to multicomponent adherence behaviors because the development of new skills or habits must compete with the elimination of old habits, routines, and preferences. Classical learning theory[58] and considerable adherence intervention research in chronic disease populations[57,59] show that new skills and habits—no matter whether they are practiced for weeks, months, or even as long as the 1-year period in the original Pocket PATH RCT—are unlikely to be sustained once ongoing reinforcement for those behaviors ends. Although apps are thought to be self-reinforcing for patients in that they promote independence and a means to self-manage one's health,[60] external sources of reinforcement largely ended at the conclusion of the Pocket PATH RCT. Namely, although LTRs kept the smartphone with the Pocket PATH app and were told they could continue using it to record and view trends in self-management activities, the data plan supporting some app features was discontinued because there were no funds for those costs. For some patients, Pocket PATH may have thereby lost its utility. There was also no funding for continued technical support services, and no one (from either the research or clinical transplant team) contacted patients to inquire about its use. Thus, patients may have felt little incentive to use it. These types of problems reflect the well-recognized practical and fiscal difficulties of transitioning from activities in a research study to routine clinical use, and are stumbling blocks that challenge even the most effective adherence-promoting interventions.[15,16]

Regardless of why Pocket PATH's use and impact were generally not sustained, our study indicates that in the cohort as a whole, nonadherence in the long-term after lung transplantation was relatively common. Patients, on average, were nonadherent to 3 of 8 assessed areas of the regimen, and nonadherence in some areas approached or exceeded 50% of the cohort. As is typical,[4,5,39,61–63] nonadherence rates worsened over time. Although nonadherence in some areas at follow-up remained rare (eg, tobacco use), relatively high rates in critical areas (eg, taking immunosuppressants, attending clinic appointments) suggest that interventions to sustain adherence well beyond the early years posttransplant are needed. In addition, the variability in nonadherence rates in the cohort across areas of the regimen—ranging from 4% (tobacco use) to 81% (spirometry)—underscores the need to identify factors that may uniquely affect risk for nonadherence in specific areas of the posttransplant regimen.[4,7]

To that end, we examined a variety of potential risk factors assessed at various points between transplant and our follow-up. Consistent with past research in organ recipients,[31,64–67] younger age generally increased nonadherence risk; this effect was statistically significant for blood pressure monitoring. Of interest, patients with more acute graft rejection episodes during the first year posttransplant were nonadherent to a greater total number of areas of the regimen and, specifically, had higher rates of nonadherence to

medications, spirometry, and blood pressure monitoring. While it might be presumed that experiencing rejection episodes would spur patients to greater adherence in these areas, patients may instead have felt they had limited ability to affect their health through their own behavior. Although our data do not bear out this latter possibility, we used only a generic measure of patients' perceived control over their health that may not have captured reactions to transplant-specific events such as graft rejection episodes. Future work should focus on patients' beliefs about their ability to prevent or modulate the impact of transplant-specific stressors to better understand how such stressors might affect their adherence.

Another important finding was that patients experiencing more chronic anxiety in the first year posttransplant were at risk for nonadherence to a greater total number of areas of the regimen and, specifically, medication non-adherence at the long-term follow-up. There are mixed data on whether psychological distress, including anxiety and depressive symptomatology, increases nonadherence risk in the early years after organ transplantation.[4,66,68–71] We know of no work examining such prediction into the longer-term years. It is possible that the anxiety-nonadherence association we observed might be connected to the occurrence of acute rejection episodes but (a) the anxiety and rejection variables were unrelated to one another (Spearman r=−0.02) and (b) in the regression analyses, each risk factor's association with the outcomes was found after controlling for all other potential risk factors in the models. In a post hoc analysis, we added an interaction term to the regression models to explore whether the anxiety and rejection episode risk factors had synergistic effects, but we found no evidence of such impact (Table S2, SDC, http://links.lww.com/TP/B775). Overall, the results suggest that chronic anxiety has a unique role as a risk factor. Interestingly, elevated anxiety symptoms at the time of the follow-up were not reliably associated with any nonadherence outcome. It may be that the experience of repeated and/or sustained bouts of elevated anxiety is what matters, and it is known that ongoing anxiety is particularly prevalent in individuals with chronic lung disease, including LTRs.[72,73] This suggests that routine screening for chronic anxiety in LTRs, followed by appropriate interventions, may have roles in promoting continued adherence.

Finally, consistent with evidence that the best predictor of current adherence is past adherence,[5,32] we found that nonadherence at the end of the first year posttransplant predicted nonadherence at follow-up for most areas of the regimen (Table 3, last column). However, these effects were not maintained once we controlled other potential risk factors. Hence, although adherence history is a relevant consideration, there may be other factors, including those we identified, that are more important contributors to nonadherence risk.

Our study has limitations. First, we could not examine differences in nonadherence based on post-RCT duration of Pocket PATH use. Such data were not prospectively collected and, at follow-up, we judged it unlikely that LTRs could reliably recall how long and in what ways they might have continued to use the app over a multi-year period. Second, because considerable time passed between the end of the original RCT and our follow-up, there may have been interim psychosocial and clinical factors other than those we examined that affected nonadherence risk. Third, our sample at follow-up was relatively small and comes from a single site, potentially limiting generalizability. Fourth, some LTRs did not participate in our follow-up because they could not be reached, refused, or were too ill. They

may have differed from follow-up participants in their long-term adherence. Finally, our focus at follow-up was necessarily on survivors. LTRs with shorter survival times may have differed in their adherence from that observed in our follow-up cohort. Indeed, we previously reported that LTRs in the original trial who failed to perform the behaviors promoted by Pocket PATH in the first year posttransplant had subsequently higher rates of mortality and BOS.[74] Nevertheless, study of nonadherence and its risk factors is important even in long-term survivors because adherence to the medical regimen remains a priority for the duration of LTRs' lives.

In conclusion, Pocket PATH did not have sustained impact on nonadherence to most areas of the regimen, although we identified other predictors of long-term non-adherence. Future work is needed not only to systematically develop and test other mHealth approaches in transplantation but also to explore strategies to facilitate interventions' sustained effects. It is likely that sustained effects can be achieved only by active continuation of intervention activities. Thus, as noted in the adherence literature in chronic disease, there is no permanent "cure" for nonadherence that would allow intervention activities to end once adherence is achieved.[57] Instead, interventions, including mHealth interventions, must become a permanent part of patients' lives for as long as they are expected to follow a medical regimen. With respect to mHealth strategies such as apps, there is growing consensus that they should be coupled with other intervention components including, for example, additional technologies such as electronic pillboxes and activity monitors that are integrated with the apps to provide more detailed behavioral feedback.[2,14,22,30]

Moreover, strategies are needed to motivate patients to continue to use apps and any other technologies integrated with them. Unfortunately, there is a dearth of theory or empirical evidence to suggest how best to motivate patients toward sustained app use.[22.30,75] Indeed, virtually all studies of mHealth interventions for health behavior change or for adherence in chronic disease focus on short-term use, with follow-up durations of well <1 year.[23,28–30] Possible strategies to facilitate long-term, sustained use include booster sessions to draw on patients' own reasons for wanting to adhere to the medical regimen, and problem-solving around barriers to app use (including, eg, financial costs of use, privacy and health information security, and app complexity).[30,76] In addition, patients themselves should be asked what they want in an app for long-term use. Although transplant recipients may view app use favorably in general or for short-term use,[10–12] research exploring their attitudes about apps' or other mHealth interventions' long-term value, and how their self-management needs evolve over time posttransplant, may be critical for formulating plans to foster continued use and sustained impact of mHealth interventions. Additionally, clinicians influence patient adoption of mHealth strategies, particularly when they are incorporated into routine clinical care,[60] and clinician feedback on app use and results may be a potent element motivating patients.[2] Thus, it will also be essential to explore how to integrate such technologies into transplant programs' workflow to optimize and sustain patient self-management.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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TABLE 1.

Instruments used to assess potential predictors and correlates of adherence

Measure[a]	Instrument and description	Instrument scoring	Cronbach's α, current sample
Baseline factors			
Sociodemographic characteristics	Standard self-report items for patients' age, sex, race/ethnicity, education, and marital status	Categories for each variable are reported in Table 2	n/a
Perceived self-care agency[b]	Perception of Self-Care Agency Questionnaire,[43] assessing patients' self-reported perceived capacity to perform self-care to manage their health	Sum of 53 items (score range, 53 [low]-265 [high self-care agency])	0.94
Locus of control for health[b]	Multidimensional Health Locus of Control Scale,[44,45] assessing patients' self-reported beliefs about whether their health outcomes were under their own control, due to chance, or due to the activity of others, including healthcare professionals	Each subscale is average of 6 items (score range, 1 [low]-6 [high locus of control]):	
		Internal Locus of Control	0.76
		External Locus of Control, Chance	0.77
		External Locus of Control, Powerful Others	0.47
		Third subscale not used in analyses due to poor alpha	
Social support from family caregiver[b]	Perceived Relationship with Family Caregiver, using self-report items adapted from the work of Spanier[46] and Pearlin and Schooler,[47] employed in other studies of transplant candidates and recipients[4,48–50]	Average of 15 items (score range, 1 [low]-5 [high support])	0.83
		Because measure was skewed, it was dichotomized to identify LTRs with low support (lower third of the distribution) vs all remaining patients	
Transplant-related medical factors	Indication for transplant, type of lung transplant, length of hospitalization after transplant, extracted from medical record	Categories and coding for each variable are reported in Table 2	n/a
Status during first y posttransplant (period of the original trial)			
Length of time rehospitalized during y	Information extracted from medical record	Count of number of d; coded into categories as reported in Table 2	n/a
Number of acute graft rejection episodes graded ≥A2	Medical record information on diagnosis of acute rejection, based on histologic examination of transbronchial lung biopsy specimens per International Society for Heart and Lung Transplantation (ISHLT) criteria in use when the specimens were graded[51]	Count of episodes, coded into categories as reported in Table 2	n/a
Development of bronchiolitis obliterans syndrome (BOS) at grade ≥1	Medical record information on diagnosis of BOS, grading based on ISHLT criteria (≥20% decrease in FEV1 relative to the mean of the two highest posttransplant FEV1 values, not explained by illness, infection or factors)[52]	Incidence of BOS present vs absent in first y posttransplant	n/a
Chronically elevated anxiety symptomatology[b]	Anxiety Subscale, SCL-90-Revised,[53] self-reported at 2, 6, and 12 mo posttransplant	Average of 10 items (score range, 0 [low]-4 [high])	0.78
		Count of number of assessments on which patients had clinically significant anxiety, defined as >1 SD above the gender-specific normative mean (ie, higher than 84% of the normative sample)[4,17,53]	

Measure[a]	Instrument and description	Instrument scoring	Cronbach's α, current sample
Chronically elevated depression symptomatology[b]	Depression Subscale, SCL-90-Revised,[53] self-reported at 2, 6, and 12 mo posttransplant	Average of 13 items (score range, 0 [low]-4 [high]) Count of number of assessments on which patients had clinically significant depression, defined as >1 SD above the gender-specific normative mean	0.81
Nonadherence to 8 areas of the medical regimen	Health Habits Survey, patient self-report, and collateral (family caregiver) separate report, assessing same areas during RCT as at follow-up assessment; see text for description of survey; data used from final assessment in RCT (12 mo posttransplant)	Coding and description of each adherence variable is described in text 11 patients were missing 12-mo assessments. Of these, 7 completed 6-mo assessments; to include them in the analyses, we imputed their missing 12-mo values by carrying the 6-mo value forward	n/a
Status after y 1 through time of follow-up assessment			
Number of acute graft rejection episodes graded ≥A2	Information extracted from medical record on acute rejection, diagnosed as described above	Count of episodes, coded into categories as reported in Table 2	n/a
Development of BOS at grade ≥1	Information extracted from medical record, diagnosed as described above	Incidence of BOS present vs absent during follow-up period	n/a
Patient had family caregiver at follow-up	Single item patient self-report	Coded as caregiver present vs absent	n/a
Social support from family caregiver[b]	Perceived Relationship with Family Caregiver, using self-report items described above	See description for social support during first y posttransplant	0.84
Chronically elevated anxiety symptomatology[b]	Anxiety Subscale, SCL-90-Revised,[53] self-reported at time of assessment	See description for anxiety during first y posttransplant	0.79
Chronically elevated depression symptomatology[b]	Depression Subscale, SCL-90-Revised,[53] self-reported at time of assessment	See description for depression during first y posttransplant	0.82

[a] All measures have been used in prior studies of transplant recipients.

[b] Multi-item rating scales. All such scales have established psychometric properties.

FEV1, forced expiratory volume in 1 second; LTR, lung transplant recipient; SCL-90, Symptom Checklist 90; SD, standard deviation.

TABLE 2.

Characteristics at baseline of original trial and during subsequent follow-up period in 105 lung transplant recipients who completed the long-term interview

Characteristic	Pocket PATH (n = 47)	Usual care (n = 58)	P^a
Time since transplant at follow-up interview, y, M (SD)	3.9 (0.9)	3.9 (0.7)	0.866
Baseline sociodemographic and psychosocial factors			
Age at transplant, y, M (SD)	56.2 (12.3)	56.0 (14.2)	0.930
Sex, % (n) male	48.9 (23)	58.6 (34)	0.322
Race/ethnicity, % (n)			0.603[b]
Nonhispanic white	93.6 (44)	87.9 (51)	
Nonhispanic black	6.4 (3)	10.3 (6)	
Hispanic	0.0 (0)	1.7 (1)	0.689[b]
Education, >high school, % (n)	95.7 (45)	93.1 (54)	
Marital status at transplant, % married or with significant other	70.2 (33)	69.0 (39)	0.890
Perceived self-care agency (53 = low; 265 = high), M (SD)	231.9 (23.2)	223.1 (24.6)	0.065
Locus of control for health (1 = low, 6 = high), M (SD)			
Internal	4.2 (1.0)	4.0 (1.0)	0.194
External: due to chance	3.1 (1.3)	3.0 (1.1)	0.466
Social support from family caregiver, low, % (n)	34.0 (16)	31.0 (18)	0.743
Baseline transplant-related characteristics			
Transplant indication, % (n)			0.108
Obstructive lung disease (non-a-1-antitrypsin deficiency)	46.8 (22)	25.9 (15)	
Pulmonary fibrosis	17.0 (8)	32.8 (19)	
Cystic fibrosis	12.8 (6)	17.2 (10)	
Other	23.4 (11)	24.1 (14)	
Type of lung transplant, % double lung (n) (vs single lung)	91.5 (43)	89.7 (52)	1.000[b]
Length of stay after transplant surgery, % (n)			0.027
≤2 wk	23.4 (11)	6.9 (4)	
>2 wk to 1 mo	46.8 (22)	44.8 (26)	
>1 mo	29.8 (14)	48.3 (28)	

Characteristic	Pocket PATH (n = 47)	Usual care (n = 58)	P^a
Status during first y after transplant[c]			
Length of time rehospitalized during y, % (n)			0.499
No rehospitalization	23.4 (11)	20.7 (12)	
≤2 wk	34.0 (16)	43.1 (25)	
>2 wk to 1 mo	10.6 (5)	15.5 (9)	
>1 mo	31.9 (15)	20.7 (12)	
Episodes of grade A2 or greater acute cellular rejection, % (n)			0.986
None	53.2 (25)	53.4 (31)	
1 episode	31.9 (15)	32.8 (19)	
2 to 3 episodes	14.9 (7)	13.8 (8)	
Anxiety, number out of 3 assessments during the y in which clinically significant symptoms were present, % (n)			0.358
0 assessments	61.7 (29)	51.7 (30)	
1 assessment	21.3 (10)	19.0 (11)	
2 to 3 assessments	17.0 (8)	30.0 (17)	
Depression, number out of 3 assessments during the y in which clinically significant symptoms were present, % (n)			0.965
0 assessments	51.1 (24)	53.4 (31)	
1 assessment	23.4 (11)	24.1 (14)	
2 to 3 assessments	25.5 (12)	22.4 (13)	
Status after y 1 through time of follow-up assessment			
Episodes of grade A2 or greater acute cellular rejection, % (n)			0.253
None	70.2 (33)	69.0 (40)	
1 episode	23.4 (11)	15.5 (9)	
2 to 3 episodes	6.4 (3)	15.5 (9)	
BOS, % (n)	21.3 (10)	31.6 (18)	0.238
Patient continued to have family caregiver at follow-up interview, yes, % (n)	66.0 (31)	84.5 (49)	0.027
Social support from family caregiver at follow-up, low, % (n)[d]	32.3 (10)	36.7 (18)	0.683
Clinically significant anxiety symptoms at follow-up interview, % (n)	38.3 (18)	39.7 (23)	0.887
Clinically significant depression symptoms at follow-up interview, % (n)	42.6 (20)	58.6 (34)	0.101
Continued to use Pocket PATH at follow-up, % (n)	4.3 (2)	–	–

[a] χ^2 test or *t* test except as noted.

[b] Exact test due to low frequencies in some cells.

[c] Although the presence of BOS was examined for this period, there were no cases in either study group.

[d] Assessed among 80 patients with a family caregiver at follow-up.

BOS, bronchiolitis obliterans syndrome; Pocket PATH, pocket personal assistant for tracking health; SD, standard deviation.

TABLE 3.

Nonadherence to elements of the post lung transplantation regimen at the end of the RCT and at long-term follow-up assessment by study group assignment, Pocket PATH vs usual care

	12-month assessment				Long-term follow-up assessment				Comparisons over time in total cohort	
Nonadherence characteristics assessed	**Total (N = 101)**	**Pocket PATH (n = 44)**	**Usual care (n = 57)**	***P*[a]**	**Total (N = 105)**	**Pocket PATH (N = 47)**	**Usual care (N = 58)**	***P*[b]**	**Did nonadherence level change from 12 mo to follow-up?[c]**	**Was nonadherence at follow-up associated with nonadherence at 12 mo (end of trial)?[d]**
Total number of nonadherent elements, M (SD)	2.0 (1.4)	1.6 (1.2)	2.3 (1.4)	0.022	2.9 (1.5)	2.7 (1.5)	3.1 (1.5)	0.218	<0.001	<0.001
Specific areas of the regimen										
Primary immunosuppressant medication (missed >1 per mo), % (n)	7.9 (8)	4.5 (2)	10.5(6)	0.460[b]	13.3(14)	6.4 (3)	19.0(11)	0.059	0.424	0.020
Nonimmunosuppressant medications (missed >1 per mo), % (n)	14.9(15)	9.1 (4)	19.3(11)	0.153	22.9 (24)	17.0(8)	27.6(16)	0.200	0.230	0.064
Clinic appointments (missed any visits in past y), % (n)	1.0(1)	0.0 (0)	1.8(1)	1.000[b]	31.4 (33)	38.3(18)	25.9(15)	0.172	<0.001	0.140
Spirometry (<several times per wk in first y posttransplant; <weekly at follow-up), % (n)	64.4 (65)	54.5 (24)	71.9 (40)	0.070	81.0(85)	80.9 (38)	81.0 (47)	0.981	0.017	0.650
Monitoring blood pressure (<several times per wk in first y posttransplant; <weekly at follow-up), % (n)	64.4 (65)	50.0 (22)	75.4 (43)	0.008	64.8 (68)	59.6 (28)	69.0 (40)	0.317	1.000	0.012
Diet (went off diet > occasionally), % (n)	17.8(18)	18.2(8)	17.5(10)	0.934	22.9 (24)	17.0(8)	27.6(16)	0.200	0.424	0.016
Exercise (< once per wk), % (n)	27.7 (28)	25.0(11)	29.8(17)	0.591	57.1 (60)	48.9 (23)	63.8 (37)	0.126	<0.001	0.008
Tobacco use (any), % (n)	1.0(1)	2.3(1)	0.0 (0)	0.436[b]	3.8 (4)	6.4 (3)	1.7(1)	0.323[b]	0.250	0.018

[a] Comparing the 2 intervention groups at the last (12-mo) assessment in the original RCT.

[b] Comparing the 2 intervention groups at the long-term follow-up.

[c] Paired *t* test to compare means and McNemar test to compare proportions. Comparisons include the 101 patients with both the 12-mo and long-term follow assessments.

[d] *t* test associated with correlation coefficient to compare total number of nonadherent elements and χ^2 test to compare proportions. Comparisons include the 101 patients with both the 12-month and long-term follow-up assessments.

Pocket PATH, pocket personal assistant for tracking health; RCT, randomized controlled trial; SD, standard deviation.

TABLE 4.

Regression analyses examining potential risk factors and correlates of long-term nonadherence, n = 101 patients with data from original trial and follow-up assessment

			Nonadherence to:									
	Total no. of areas of nonadherence		Taking medications		Attending clinic appointments		Performing spirometry		Monitoring blood pressure		Following diet/ exercise requirements	
Potential risk factors or correlates[a,b,c]	**β**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**
Stage 1: Patient status at RCT baseline												
Younger age at transplant, y	0.02	−0.01–0.04	1.01	0.97–1.04	1.02	0.99–1.05	1.04	0.99–1.09	**1.04**	**1.01–1.09**	0.98	0.95–1.01
Poorer caregiver support	−0.04	−0.68–0.59	0.36	0.11–1.16	0.90	0.37–2.22	2.07	0.62–6.93	0.83	0.33–2.06	1.31	0.53–3.23
Longer length of hospital stay after transplant	0.10	−0.32–0.53	1.39	0.68–2.84	1.07	0.58–1.97	0.73	0.34–1.56	1.63	0.88–2.99	0.94	0.53–1.74
Stage 2:[d] Patient status during first y posttransplant (period of original RCT)												
Group assignment, Pocket PATH	0.10	−0.49–0.69	0.58	0.18–1.87	2.10	0.85–5.23	0.84	0.27–2.57	1.10	0.38–3.13	**0.38**	**0.15–0.98**
Longer total rehospitalization time during first y	−0.01	−0.28–0.25	0.73	0.43–1.23	1.31	0.87–1.96	0.99	0.59–1.66	**0.47**	**0.29–0.78**	1.26	0.80–1.99
Greater number of episodes of A2 or greater acute rejection during first y	**0.47**	**0.08–0.86**	**2.68**	**1.24–5.80**	0.97	0.52–1.79	**3.07**	**1.17–8.03**	**2.10**	**1.03–4.28**	1.62	0.82–3.19
Greater number of assessments indicating clinically significant anxiety during first y	**0.36**	**0.07–0.65**	**2.30**	**1.29–4.10**	1.33	0.86–2.07	1.17	0.66–2.10	1.65	0.98–2.80	1.42	0.88–2.29
Nonadherence at 1 y (end of trial)[e]	0.21	−0.03–0.45	2.31	0.57–9.36	-	-	1.13	0.36–3.51	2.47	0.89–6.88	**3.11**	**1.08–8.99**
Stage 3:[d] Patient status at time of follow-up assessment												
Clinically significant anxiety at follow-up assessment	0.19	−0.45–0.83	0.90	0.27–2.99	1.93	0.72–5.17	1.47	0.42–5.16	0.73	0.24–2.20	0.68	0.23–2.05
R^2 for complete model[f]	0.22		0.31		0.13		0.19		0.32		0.27	

[a]Other variables that did not meet criteria for inclusion in final models were sex, race/ethnicity (non-Hispanic white vs all other groups), marital status at transplant, perceived self-care agency, internal locus of control, external locus of control, indication for transplantation, persistent depression during the first year posttransplant, acute rejection after the first year posttransplant, BOS, whether the patient had a family caregiver at follow-up, and the supportiveness of that relationship. Education and type of lung transplant were not eligible for inclusion due to very limited variability on these variables in the sample.

[b]Although both clinically significant anxiety at follow-up and clinically significant depression at follow-up both met inclusion criteria for the final models, they were highly intercorrelated (r = 0.69) and thereby introduced a multicollinearity problem and instability in model parameter estimates (very large confidence intervals).[51] We chose to report the model with anxiety at follow-up given that earlier levels of anxiety were also included in the models. However, repeating the modeling with depression at follow-up instead yielded similar results: it was not a statistically significant factor in any model

[c] Factors with significant ($P < 0.05$) associations with outcomes are shown in bold font.

[d] For each outcome, the Stage 2 model adjusts for predictors entered at Stage 1, and the Stage 3 model adjusts for predictors entered at Stages 1 and 2.

[e] For each outcome, this predictor reflected previous nonadherence in the same area as the outcome (eg, previous medication taking if the outcome was medication-taking at follow-up). Nonadherence to clinic appointment attendance could not be included as a predictor because only 1 patient reported nonadherence in this area in the original RCT.

[f] R^2 for linear regression (for total number of 8 areas of nonadherence) and Nagelkerke R^2 for logistic regressions (individual nonadherence outcomes).

BOS, bronchiolitis obliterans syndrome; CI, confidence interval; OR, odds ratio; Pocket PATH, pocket personal assistant for tracking health; RCT, randomized controlled trial.