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A multi-component, family-focused and literacy-sensitive intervention to improve medication adherence in patients with heart failure—A randomized controlled trial

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ABSTRACT

Background: Medication nonadherence is prevalent and links to serious outcomes (e.g., rehospitalization/death) in heart failure (HF) patients; therefore, an urgent need exists for an intervention to improve and sustain adherence after intervention completion.
Objectives: To test the efficacy of a multi-component, family-focused, literacy-sensitive (*FamLit*) intervention on medication adherence in HF patients.
Methods: Forty-three HF patients and their care partners were enrolled and randomized to receive FamLit or attention-only intervention, including an in-person session at baseline and bi-weekly phone boosters for 3 months. We measured medication adherence from baseline to 3-month post-intervention using the Medication Event Monitoring System.
Results: After 3-month intervention, intervention patients had significantly better medication adherence than control patients. At 6 months (3-months post-intervention), intervention effect on adherence was sustained in the FamLit intervention group, while adherence decreased in the control group.
Conclusion: Incorporating care partner support and providing an easy-to-understand intervention to patients-care partners may improve/sustain adherence.

Heart failure (HF) is a chronic condition and a serious public health threat: 6500,000 Americans have HF and about 300,000 die each year.[1,2] Despite advances in medical therapy, the death rate remains high, with an estimated 50% of patients dying within five years of HF diagnosis.[1,3] Hospitalization rates are high in patients with HF, and 67% were readmitted within one year of discharge for exacerbations of HF.[4,5] HF is also the most costly cardiovascular illness in the United States: annual total costs were $30.7 billion in 2012 and are projected to be $69.7 billion by 2030.[2]

Appropriate therapy can modify the natural history of HF, but medication adherence is essential to realize this benefit.[6,7] Poor adherence to prescribed medications is a substantial problem, and is linked to unnecessary hospitalizations, increased emergency department (ED) visits,[8] excessive medical costs,[6,7] increased mortality, and poor quality of life.[9] Thus, it is crucial to maximize medication adherence in patients with HF.

Many patients with HF need support from care partners (i.e., family, relatives, partners, close friends) to manage their HF better, such as providing transportation to medical appointments, sorting prescribed medications in their pillbox, preparing a low salt diet, and following medical regimens.[10,11] The care partner/family interventions have improved medication adherence and reduced hospitalizations in patients across several chronic conditions, such as hypertension,[12] diabetes,[13,14] cancer,[15,16] psychosis,[17] and substance abuse.[18] Through the few intervention studies examining care partners/families and self-care in HF,[19] we know that care partner/family interventions increased patient-care partners' understanding of each other's experiences and improved self-care in general,[20] and improved adherence to a low sodium diet[21] and medication adherence.[22] These findings demonstrate the potential promising effects of care partner/family interventions in improving self-care adherence in HF.

Low health literacy is associated with a higher risk of hospitalization among patients with HF.[23] Adequate literacy is important for adherence to complicated medical recommendations. Adults with basic and less than basic literacy have difficulty understanding health

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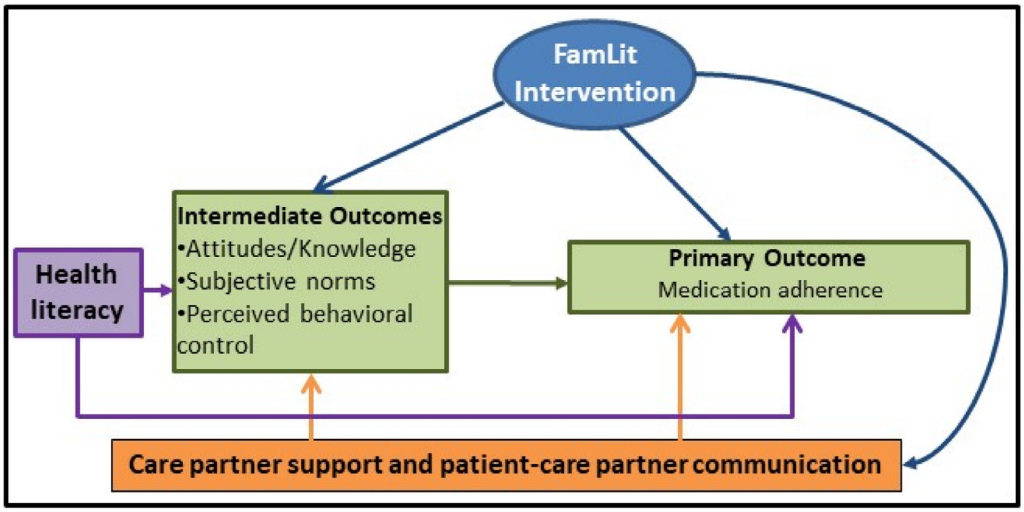

Fig. 1. Conceptual framework. The Family-focused, Literacy-sensitive (FamLit) intervention uses multiple strategies that are easy to understand to target three constructs of the Theory of Planned Behavior (TPB): attitudes, subjective norms, and perceived behavioral control, as well as enhance care partner support and patient-care partner communication to improve and sustain patient medication adherence.

information.[24] In one study, HF patients indicated they did not understand information provided by their healthcare providers, resulting in poor medication adherence.[25] Low health literacy is prevalent (27–54%) in patients with HF.[26] The National Assessment of Adult Literacy[24] found that 29% had basic literacy (i.e., the skills necessary to perform simple and everyday activities), and 14% had less than basic literacy (i.e., can perform only the most simple and concrete skills). Implementation of interventions that can be understood by HF patients with low literacy is imperative to maximize adherence to complex health regimens.

Both care partner support and health literacy are predictors of medication adherence.[27,28] HF patients with low health literacy are more likely to bring care partners to medical appointments to seek health information.[29] Many patients with HF are elderly and rely on the help of care partners.[25] These study findings underscore a need to integrate Family-focused and Literacy-sensitive (FamLit) strategies to improve adherence in HF patients. Accordingly, we tested the efficacy of a FamLit intervention to improve medication adherence in patients with HF.

Conceptual framework (Fig. 1)[30,31]

Because we approached the problem of improving medication adherence as both being multi-faceted and dependent on care partner support, the integration of two relevant theoretical frameworks addresses these issues. The study's conceptual framework integrates the Theory of Planned Behavior (TPB)[30] (green) with Lee's model of care partner support[31] (orange), and links health literacy to health outcomes. The TPB, with three constructs —attitudes/knowledge, subjective norms, and perceived behavioral control—is commonly used in studies to change/improve health behaviors, including medication adherence.[30] **Attitudes/ knowledge** are the individual's beliefs about the outcomes of adhering to prescribed medications, weighted by whether the individual considers those outcomes essential.[30] **Subjective norms** are care partners' beliefs about the importance of medication adherence and their approval or disapproval, support or lack of support of medication adherence,[30] weighted by the level of the individual's motivation to comply with the approval/disapproval of care partners.[30] **Perceived behavioral control** reflects patients' and care partners' perceived barriers, such as financial needs/distress and the presence or absence of resources for taking prescribed medications, weighted by the perceived impact of barriers and resources (e.g., costs of refilling the prescriptions or making other purchases).[30] Patients with low **health literacy** (purple) had poorer ability to understand commonly-used prescription medication labels[32] and medication warning labels.[33] In addition, low health literacy was associated with poor self-care behaviors, and increased hospitalizations and death.[26,34]

Lee's model posits that **care partner support** may alleviate the adverse effects of low health literacy in which low health literacy patients with more care partner support improve their ability to obtain, understand and apply medication information, thus promoting healthy behaviors and reducing hospitalization.[35,36] We therefore developed the FamLit intervention (blue) targeting patients' and their care partners' attitudes/knowledge, subjective norms, and perceived behavioral control and facilitating patient-care partner communication and support to improve patient medication adherence and outcomes. FamLit includes easy-to-read intervention materials and "Teach-To-Goal" strategies. In this study, we tested whether the FamLit intervention improved and sustained medication adherence using multiple complementary strategies: HF specific instruction, coaching, role playing, teach-back, and goal setting. We hypothesized that patients who received the multi-component FamLit intervention would demonstrate better medication adherence than the control group, and that the intervention effect would be sustained for three months after intervention completion.

Methods

Design

This was a 2-group, randomized controlled trial. We tested the efficacy of a 3-month, multi-component, FamLit intervention on patient medication adherence.

Sample and setting

The study took place at an academic medical center in the southeastern United States. We screened potential participants' pre-intervention medication adherence to determine whether their medication adherence was optimal or sub-optimal as measured by a validated single item question about whether they had any missed dose of their prescribed heart medication in the prior 7 days.[37] Only patients with sub-optimal adherence, defined as having missed at

least one dose of HF medicine in the prior 7 days, and their care partners were included in the study. A total of 43 HF patients and their care partners were enrolled. The sample size was determined by power analysis considering an attrition rate of 20%. With 20 patients in each group and an alpha level of 0.05, the power of the 2-sample *t*-test to detect a group difference in change in medication adherence using the data from the Medication Event Monitoring System (MEMS) is 80% when the ratio of the difference in means to the standard deviation is 0.9.

Inclusion criteria for patients

Patients had to meet several inclusion criteria: 1) confirmed diagnosis of HF; 2) have a primary care partner (spouse, daughter/son, or other relative/close friend who involved in patient's HF care) identified by the patient as the person most involved in their HF care; 3) missed at least one dose of HF medicine in the prior 7 days; 4) have stable doses of HF medications for at least 3 months; 5) reside in a setting where the patient was responsible for his/her own medication administration; 6) aged 21 years or older; and 7) have a working landline or cell phone.

Patients were excluded for: 1) cognitive impairment measured by the Mini-Cog Exam, a three-word recall test and a clock-drawing test; those with a word recall score of 0 or a word recall of $\leq$2 and an abnormal clock test (i.e., inability to place the hands of the clock correctly to represent a designated time) were excluded; 2) co-existing terminal illness such as end-stage renal disease, advanced malignancy, or any other condition with <1-year life expectancy; 3) receiving hospice care; 4) psychotic illness; 5) current alcohol dependence or other substance abuse; or 6) inability to speak English or other communication barrier.

Inclusion criteria for care partners

Care partners were eligible if they 1) were the primary, non-paid partners of a community-dwelling patient with HF living at home; 2) were willing to receive interventions with the patient; and 3) were 21 years of age or older.

Care partners were excluded for 1) cognitive impairment, measured by the Mini-Cog Exam; 2) diagnosis of a terminal illness; or 3) inability to speak English or other communication barrier.

Procedure

We obtained permission to conduct this study from the appropriate Institutional Review Board. Healthcare providers at the clinic recruitment site referred patients to the study. A research assistant met with patients and their care partners at the clinic and explained study requirements. If the patient and care partner met eligibility criteria and consented to participate, baseline data were collected. We then randomized patients and their care partners by concealed allocation based on a random number generator to receive the FamLit intervention or equal attention-only intervention. All patients were followed for 6 months (3-month intervention plus 3 months post-intervention follow-up) from baseline.

Intervention

The family focus of the FamLit intervention is designed to help patients-care partners learn the importance of working together to achieve medication adherence.[14,15] The intervention emphasized skill building (understanding, communication, and support) and patient-care partner team work as the prime methods of improving medication adherence. Skills were developed through increasing the patient-care partner's knowledge of HF specific symptoms and treatment and that knowledge was confirmed by asking patients-care partners to teach-back, and through discussion, coaching, practice, and roleplay in providing appropriate emotional/practical support and overcoming barriers to medication adherence. With perceptions of increased support and improved communication and strengthened perceived behavioral control, we expected medication adherence to improve, and the positive effect sustained with continuing support from the care partner.

To be literacy-sensitive, the FamLit intervention used an intervention guide that could be easily understood by those with low health literacy but was also appealing to people with higher health literacy. We also used the "Teach-To-Goal" (TTG) approach to provide longitudinal support, a well-established and effective intervention developed by health literacy experts for HF patients with low health literacy.[38] Although most heath behavior theories assume that people clearly understand the information provided by the healthcare provider, in reality, many patients and their care partners do not understand the instructions. Literacy-sensitive approaches recognize that people with different levels of health literacy learn at different rates, but the vast majority can master material if they have more opportunities to be given instructions at their level of understanding and more opportunities to ask questions, clarify their concerns, and practice by roleplaying. A TTG intervention gives each patient-care partner multiple opportunities to improve their understanding until they reach full understanding and have the skills they need to improve their medication adherence.

The multi-component FamLit intervention was delivered by a trained interventionist with expertise in cardiovascular care using the FamLit intervention guide, which was given to each patient-care partner in the FamLit intervention group to take home. *The FamLit intervention guide* was originally developed based on information from prior studies,[25,39] guidelines published by the American Heart Association,[40] pamphlets from the Heart Failure Society of America, and the experience of our research team for a theory-based intervention to improve medication adherence for patients with HF.[41] We further revised and adapted the guide to make the content suitable and inclusive for both patients and their care partners with low literacy and appealing for those with high literacy. Three experts in medication adherence, health literacy, and family studies in HF evaluated the content, as well as five pairs of HF patients and their care partners. The Guide is written at 4th-grade level and is thus "easy to understand" as assessed by Flesch-Kincaid Grade Level and the Flesch Reading Ease scale.[42]

The interventionist used the FamLit intervention guide in the in-person and phone booster sessions. The guide included strategies to: 1) build positive attitudes toward medication adherence by discussing the relationship between HF symptoms and treatment and the importance of medication adherence; 2) coach patients-care partners to learn and practice how to better communicate with and support each other to work together as a team, build positive subjective norms and enhance communication and support; 3) elicit barriers and major concerns about adhering to medications; 4) help patients-care partners with decision making through discussion of the pros and cons of making a behavior change, and provide a menu of potential solutions to overcome patients-care partners' barriers and concerns; and (5) coach the patient-care partner in setting specific goals to increase their motivation and reinforce when any goal is met.

The intervention had four pre-specified intervention goals. ***Intervention Goal 1*** was to use HF specific instruction and the teach-back strategy to encourage positive **attitudes and knowledge**, patients-care partners demonstrated basic understanding of HF, HF symptoms, HF medications and medication adherence. The interventionist explained HF and HF symptoms, described how suboptimal medication adherence results in HF symptoms, discussed the importance, benefits and positive outcomes of medication adherence, and asked patients-care partners to teach back to evaluate their understanding

and clarify any misunderstanding. ***Intervention Goal 2*** was to use coaching and role playing to build positive **subjective norms** and enhance **patient-care partner communication and support**. Patients-care partners learned and demonstrated how to communicate and support regular and continuous patient adherence to medications. The interventionist engaged patients-care partners in role playing to learn and practice how to communicate and support each other to work together as a team continuously. ***Intervention Goal 3*** was to use coaching and role playing to increase **perceived behavioral control** of medication adherence and **tailor to individualized barriers**. Patients-care partners identified and used appropriate strategies to overcome their individualized barriers to medication adherence. The interventionist helped patients-care partners identify barriers to medication adherence such as forgetting, lack of motivation, or distrust in the provider, and then explore strategies to address/eliminate those barriers, using scenarios to engage patients-care partners in practicing how to overcome their specific barriers. ***Intervention Goal 4*** was to **set attainable goals** for better medication adherence by enhancing patient-care partner's **motivation** to improve medication adherence. The interventionist and patient-care partners set specific and attainable goals/action plans jointly for better medication adherence in daily routine. To determine whether these intervention goals were reached, we required patients and care partners to answer 10 questions on our checklist correctly/appropriately.

Patients-care partners in the FamLit intervention group received a 45–60 min in-person intervention session at baseline. Together, the interventionist and patient-care partner reviewed the FamLit intervention guide that incorporated multiple components to achieve the four intervention goals. Phone sessions occurred one week after the in-person session to continue to work with patients-care partners on improving attitudes/knowledge, subjective norms, communication, support, and perceived behavioral control, and to raise their questions/concerns and to confirm their understanding/implementation of the content and skills coached/practiced in the in-person session. Interventionists using a script continued bi-weekly phone sessions until patients and care partners accomplished the four intervention goals.

All patients-care partners continued with their usual HF care from their physician or HF specialist/nurse practitioner. In order to equalize the attention provided to the two groups (FamLit and control groups) and reduce potential confounding, patients-care partners in the attention control group were given same amount of time as patients-care partners in the intervention group. Therefore, patients-care partners in the control group had one in-person session focusing on patient's general health, and they were free to interact with the nurse interventionist and ask any topics the patients-care partners want to discuss. Patients-care partners also received bi-weekly phone calls to address any concerns they had related to patient's general health.

Measures

Medication adherence

The primary outcome of the FamLit intervention is medication adherence. Because there is no "gold standard" measure of medication adherence, we used a self-reported measure (4-item Morisky Medication Adherence Scale [MMAS-4])[43] to assess medication adherence at baseline. Although a self-reported measure was adequate for baseline assessment, given its limitations such as recall bias, we used a valid and sensitive electronic monitoring device, the Medication Event Monitoring System (MEMS) to evaluate the FamLit intervention effect ***objectively*** on medication adherence over time.[44] The MEMS includes a medication bottle and a MEMS cap equipped with a microchip registering the date and time of each cap opening.[45] We used the MEMS data to calculate medication adherence: percent prescribed doses taken (# of doses taken during monitoring period/# of prescribed doses during the monitoring period $\times$ 100).[35,39]

Process measures

Process measures included patients' and care partners' indicators of the Theory of Planned Behavior (TPB; attitudes/knowledge, subjective norms, and perceived behavioral control), patient-care partner communication and perceived support. We assessed indicators of the TPB using the Medication Adherence Scale (MAS),[46] which consists of 18 items in three subscales measuring the three constructs of the TPB. Participants rated how much they agreed/disagreed with each item on Likert-type scales; we calculated scores for each subscale. We assessed patient-care partner communication using the 6-item Family Assessment Device (FAD) Communication subscale,[47,48] and measured perceived support using the 12-item multidimensional perceived social support scale (MPSSS).[49,50] These scales have adequate reliability and validity with HF patients.[19,47,48]

Other variables of interest

We collected data on demographic and clinical variables to characterize the sample, compare groups, and allow statistical considerations of any observed group differences at baseline.

Demographics

We collected data via interview on patients' and their care partners' age, gender, race, marital status, care partner relationship, residence (alone or with other), education level, and household income.

Clinical characteristics

Through interviews and medical record review, we collected data on patients' left ventricular ejection fraction, time since diagnosis of HF, body mass index, New York Heart Association functional class, comorbidities, and current medications.

Data analysis

We performed all data analyses were using SPSS, version 25 (Armonk, NY) and set a significance level of 0.05 throughout. Each participant was assigned an ID. After double-entering data collected on paper forms, we ran frequencies to find and manage exceptional values, and ran all subsequent analyses on the corrected database. We downloaded MEMS data to an encrypted, password protected computer and stored the data on a protected server. We conducted separate analyses of continuous and dichotomized data, using 80% of prescribed doses taken as the cutpoint to define medication adherence.

We followed an intent-to-treat strategy for data analyses. We compared demographic and clinical characteristics across study arms, including frequency distributions, percentage, means and standard deviations, *t*-tests and chi-squares, as appropriate to the level of measurement of the variables. Using repeated measure analysis of variance (ANOVA), we compared medication adherence between groups over the 6-month period, and also used to compare the scores of three indicators of TPB (attitudes/knowledge, subjective norms, and perceived behavioral control), patient-care partner communication, and perceived support between groups over time. We used Cohen's d to calculate the effect size of the FamLit intervention.

Results

Sample characteristics

The CONSORT flow chart (Fig. 2) reflects recruitment/randomization/attrition from groups. We approached 230 HF patients, of whom 99 were eligible based on medication adherence and presence of eligible care partner. Of the 99 eligible HF patients-care partners, we enrolled a total of 47 at baseline, with a 91% (43 patients-care partners) retention rate. Reasons for refusal to participate included time concerns (e.g., care partners had to work), no interest, long travel distance, or lack of energy. Patients' mean age was 66 ± 11 years, and 42% were female. The participating care partners were predominately spouses; adult children comprised the next largest category. Care partners ranged in age from 22 to 87 years, with a mean age of 55.2 ± 15.3, and 71% were women, 52% were African American, and 48% had high school or less education. Table 1 contains full patient characteristics and comparisons between groups. Groups did not differ on demographic and clinical characteristics at baseline.

Intervention effect on medication adherence

At baseline, there was no difference between the groups in self-reported medication adherence (0.9 vs. 1.1, p = .35). After the 3-month intervention (in-person and phone boosters), FamLit intervention group patients had better medication adherence than those in the attention control group (87.6% vs. 80.9%). The effect size of the FamLit intervention is 0.37. Compared with control group patients, FamLit intervention group patients also had better medication adherence at 6 months (87.8% vs. 74%) (Fig. 3). Repeated measure ANOVA showed a significant interaction for group by time (F = 5.003, p = .03), indicating medication adherence was sustained in the intervention group but decreased in the control group over time (Fig 3).

We then analyzed medication adherence as a dichotomized variable, and classified patients as adherent if patients' medication adherence rate was ≥80%, and as nonadherent if <80%. We chose the 80% cutpoint because this is the most common value use to define medication adherence in the current literature.[51,52] At 3 months (completion of the intervention), 78% of the patients in the intervention groups were adherent compared to only 60% of the patients in the control group (p = .21). At 6 months (3 months post-intervention), the percentage of adherent patients increased in the FamLit intervention group, while there was no change in the control group (83% vs. 60%, p = .11), although the difference did not reach statistical significance.

Process measures are the patient's and care partner's three indicators of the TPB (attitudes/knowledge, subjective norms, perceived behavioral control), patient-care partner communication and perceived support from baseline to 6 months. From repeated measures ANOVA, there was a non-significant trend toward improvement

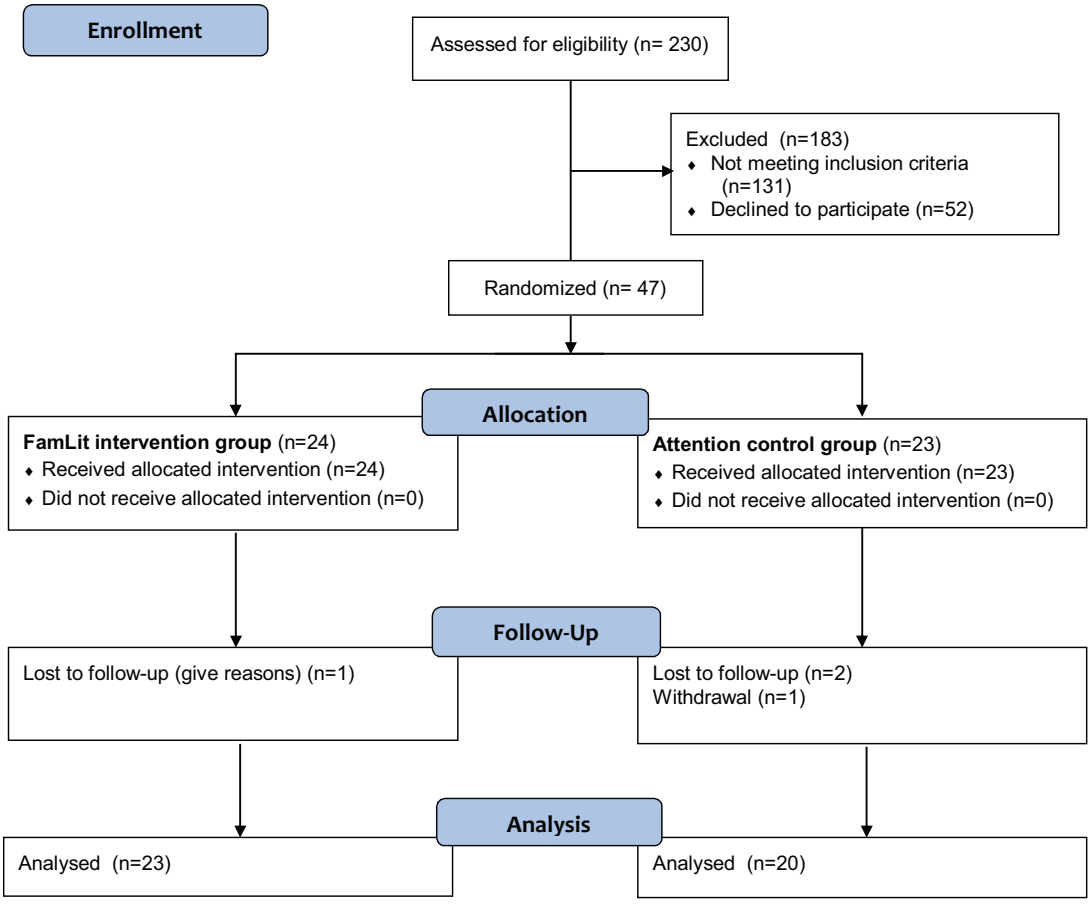

Fig. 2. FamLit CONSORT Flow Chart.

Table 1
Patient characteristics and comparisons between groups.

Characteristics	Total sample $N = 43$	Intervention $n = 23$	Control $n = 20$	p Value*
Age, years (Mean ± SD)	66 ± 11	65 ± 12	67 ± 9	.663
Female	18 (42%)	12 (52%)	6 (30%)	.142
Race, Black	26 (61%)	16 (70%)	10 (50%)	.191
Education, years (Mean ± SD)	12 ± 3	13 ± 3	12 ± 3	.179
Marital status, Married/cohabitate	25 (58%)	12 (52%)	13 (65%)	.485
Living with others	35 (81%)	18 (78%)	17 (85%)	.571
BMI (Mean ± SD)	34 ± 7.7	33.4 ± 7.4	34.7 ± 8.3	.588
LVEF, (Mean ± SD),%	42 ± 17.7	39.6 ± 19.2	44.9 ± 17.1	.576
NYHA functional class, III/IV	15 (35%)	7 (30%)	8 (40%)	.757
I/II	28 (65%)	16 (70%)	12 (60%)	
Charlson comorbidity index (Mean ± SD)	4.3 ± 2.6	4.8 ± 3.1	3.8 ± 1.9	.198
Taking ACEI	25 (58%)	14 (61%)	11 (55%)	.697
Taking BB	37 (86%)	18 (78%)	19 (95%)	.114
Health literacy (Mean ± SD)	29.4 ± 8.3	29.1 ± 9.3	29.7 ± 7.2	.802

across 6 months in the FamLit intervention group in these process measures: patient attitudes/knowledge, care partner attitudes/knowledge, care partner perceived behavioral control, care partner perceived support, but the attention control group showed little change, no change, or lower scores from baseline to 6 months (3 months post-intervention) (Table 2).

Discussion

Poor medication adherence results in HF exacerbation and subsequent hospital readmission,[6,8] and a recent systematic review and meta-analysis confirmed this.[9] In our study, we developed and tested a multi-component FamLit intervention to improve and sustain medication adherence in patients with HF.

Our findings are promising in four ways. First, we demonstrated that after intervention completion, medication adherence was significantly higher in patients in the FamLit group at 3 months compared with those in the control group. Meta-analytic evidence has demonstrated that many medication adherence intervention trials improve medication adherence in patients with HF[53]; however, the effect size for these trials was small (Cohen $d = 0.29$). In our study, in addition to showing medication adherence in the intervention group was better

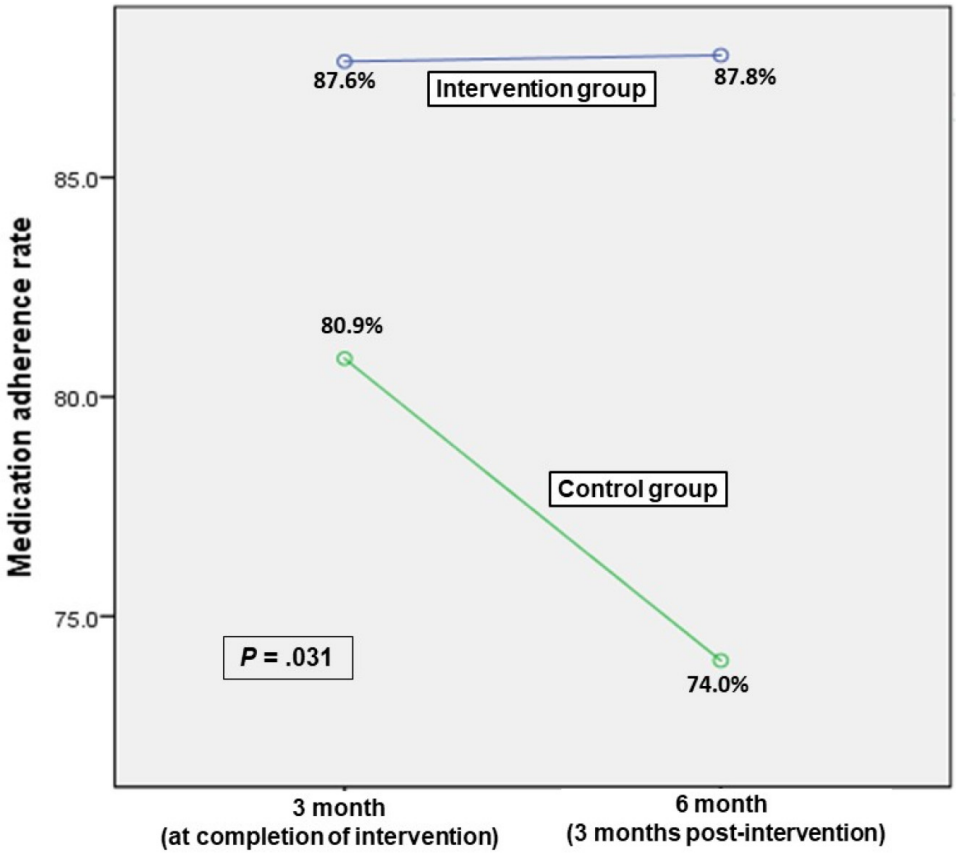

Fig. 3. Medication adherence between groups over time ($N = 43$): At the end of 3 months (at completion of the intervention), the intervention group had better medication adherence than the control group (87.6% vs. 80.9%). Repeated measures ANOVA showed a significant group-by-time interaction indicated that medication adherence was sustained in intervention group patients at the end of 6 months (3 months post-intervention), but decreased in the control group over time ($p = .031$).

Table 2
Process measures between groups.

	Process measure	Intervention (Baseline→ 3 months)	Control (Baseline→ 3 months)	*p*
Patient	Attitudes/Knowledge	20 → 22	16 → 17	.151
Care partner	Attitudes/Knowledge	23 → 25	21 → 21	.382
	Perceived behavioral control[a]	35 → 22	34 → 41	.632
	Perceived support	67 → 70	64 → 65	.454

[a] Perceived behavioral control: higher scores indicated higher perceived barriers and lower perceived behavioral control.All others: higher scores, more positive attitudes/knowledge, more perceived supportScore ranges of the scales:Attitudes/Knowledge: 0–30; Perceived behavioral control: 0–120; Perceived support: 12–84.

than the control group, the effect size of our FamLit intervention is 0.37 using Cohen's d, which is superior to the average effect size of 0.29 in the current literature.[53]

Second, when we dichotomized patients using the 80% cutpoint to define medication adherence, more patients in the intervention group became adherent compared with those in the control group at 3 months (78% vs. 60%) and at 6 months (83% vs. 60%). The findings provide further support of the effectiveness and sustainability of our FamLit intervention.

Third, only one prior study evaluated the post-intervention effect of medication adherence using the MEMS in HF[54] and an interdisciplinary team. Lasting nine months, the intervention effects were evident only during the intervention period, not 3 months after intervention completion.[54] The intensity and limited effectiveness suggests this intervention would not be feasible in usual practice settings. Our FamLit intervention includes one in-person session (45–60 min) and then multiple phone booster sessions and therefore is more feasible and transferrable to current clinical settings. If during a clinic visit a healthcare provider assesses and identifies a patient to be at risk for poor medication adherence, the provider can offer in-person session of the FamLit intervention during that visit and offer follow-up phone boosters to help the patient and care partner to work together to improve and sustain the patient's medication adherence.

Finally, and most importantly, patients in the FamLit group, medication adherence not only was better immediately after completion of intervention, but the intervention effect also was sustained 3 months post-intervention compared with the control group. In our previous study using the TPB theory-based intervention, patients in the intervention group had significantly better medication adherence than those in the control group; however, improved adherence in the intervention group decreased 3 months post-intervention.[41] If findings of this study using the FamLit intervention are verified in a larger study, this will be the first intervention demonstrating not only better medication adherence among HF patients in the intervention group *during* the intervention period, but the intervention effect *is sustained* 3 months once the intervention ends.

Our results indicate that the effect of the FamLit intervention on medication adherence may occur through increasing patient and care partner attitudes/knowledge, care partner perceived control and care partner perceived support. Although not statistically significant (likely a function of our small sample size), process measures improved from baseline to 3 months in the FamLit intervention group compared to the control group. These findings are consistent with the tenets of the TPB, thus suggesting that increased understanding, positive attitudes, improved behavioral control and support of care partners led to better patient medication adherence at both 3 and 6 months for patients in the FamLit intervention group.

Limitations

Our study has following limitations. First, our findings may apply only to those HF patients who have involved care partners. We acknowledge that HF patients without care partner involvement may be at higher risk of poor adherence and outcomes; however, our goal is to enhance naturally occurring support, suggesting that different interventions may be needed to improve and sustain medication adherence for those without care partner involvement. Second, we assumed that patients removed and took one dose of their prescribed medication after each MEMS cap opening. This is a standard assumption when using any electronic monitoring devices to measure medication adherence[44] although this assumption can be questioned. We acknowledge that there is no "perfect measure" of medication adherence, however, the MEMS has been used widely as the "reference measure" of medication adherence in current literature.[44] Without serum drug levels, we cannot ascertain if patients indeed removed the medication and took it when they opened the MEMS cap. Finally, we recruited only a small sample of 43 patients-care partners in one southeastern tertiary hospital. Although we demonstrated significantly better medication adherence in the intervention group than the control group, findings from this study warrant further study in a larger sample size to verify and generalize the results.

Conclusion

Baseline self-reported medication adherence did not differ between groups. Patients who received the FamLit intervention, compared with the attention control group, showed better medication adherence at 3 months (immediately upon completion of the intervention) and the intervention effect was sustained at 6 months (3 months post-intervention). We recommend further research to verify the findings of this study on the efficacy of the FamLit intervention in patients with HF in a larger, multi-site randomized controlled trial.

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Declaration of conflicting interests

The authors declare that there is no conflict of interest.

References

1. Benjamin EJ, Blaha MJ, Chiuve SE, et al. Heart disease and stroke statistics-2017 update: a report from the American Heart Association. *Circulation*. 2017;135:e146–e603. https://doi.org/10.1161/cir.0000000000000485.
2. Benjamin EJ, Virani SS, Callaway CW, et al. Heart disease and stroke statistics-2018 update: a report from the American Heart Association. *Circulation*. 2018;137:e67–e492. https://doi.org/10.1161/cir.0000000000000558.
3. Lloyd-Jones D, Adams RJ, Brown TM, et al. Heart disease and stroke statistics–2010 update: a report from the American Heart Association. *Circulation*. 2010;121:e46–e215. https://doi.org/10.1161/CIRCULATIONAHA.109.192667.

4. Dharmarajan K, Rich MW. Epidemiology, pathophysiology, and prognosis of heart failure in older adults. *Heart Fail Clin*. 2017;13:417–426. https://doi.org/10.1016/j.hfc.2017.02.001.
5. Dharmarajan K, Hsieh AF, Kulkarni VT, et al. Trajectories of risk after hospitalization for heart failure, acute myocardial infarction, or pneumonia: retrospective cohort study. BMJ. 2015;350:h411. https://doi.org/10.1136/bmj.h411.
6. Li H, Morrow-Howell N, Proctor EK. Post-acute home care and hospital readmission of elderly patients with congestive heart failure. *Health Soc Work*. 2004;29:275–285. https://doi.org/10.1093/hsw/29.4.275.
7. Sokol MC, McGuigan KA, Verbrugge RR, Epstein RS. Impact of medication adherence on hospitalization risk and healthcare cost. *Med Care*. 2005;43:521–530.
8. Hope CJ, Wu J, Tu W, Young J, Murray MD. Association of medication adherence, knowledge, and skills with emergency department visits by adults 50 years or older with congestive heart failure. *Am J Health Syst Pharm*. 2004;61:2043–2049.
9. Ruppar TM, Cooper PS, Mehr DR, Delgado JM, Dunbar-Jacob JM. Medication adherence interventions improve heart failure mortality and readmission rates: systematic review and meta-analysis of controlled trials. *J Am Heart Assoc*. 2016;5. https://doi.org/10.1161/jaha.115.002606.
10. Riegel B, Moser DK, Anker SD, et al. State of the science: promoting self-care in persons with heart failure: a scientific statement from the American Heart Association. *Circulation*. 2009;120:1141–1163. https://doi.org/10.1161/CIRCULATIONAHA.109.192628.
11. Rosland AM, Heisler M, Choi HJ, Silveira MJ, Piette JD. Family influences on self-management among functionally independent adults with diabetes or heart failure: do family members hinder as much as they help? *Chronic Illn*. 2010;6:22–33. https://doi.org/10.1177/1742395309354608.
12. Morisky DE, Levine DM, Green LW, et al. Five-year blood pressure control and mortality following health education for hypertensive patients. *Am J Public Health*. 1983;73:153–162.
13. Armour TA, Norris SL, Jack Jr. L, Zhang X, Fisher L. The effectiveness of family interventions in people with diabetes mellitus: a systematic review. *Diabet Med*. 2005;22:1295–1305. https://doi.org/10.1111/j.1464-5491.2005.01618.x.
14. Cole I, Chesla CA. Interventions for the family with diabetes. *Nurs Clin North Am*. 2006;41:625–639. https://doi.org/10.1016/j.cnur.2006.07.001. vii.
15. Given B, Sherwood PR. Family care for the older person with cancer. *Sem Oncol Nurs*. 2006;22:43–50. https://doi.org/10.1016/j.soncn.2005.10.006.
16. Hudson PL, Aranda S, Hayman-White K. A psycho-educational intervention for family caregivers of patients receiving palliative care: a randomized controlled trial. *J Pain Symptom Manag*. 2005;30:329–341. https://doi.org/10.1016/j.jpainsymman.2005.04.006.
17. Bird V, Premkumar P, Kendall T, et al. Early intervention services, cognitive-behavioural therapy and family intervention in early psychosis: systematic review. *Br J Psychiatry*. 2010;197:350–356. https://doi.org/10.1192/bjp.bp.109.074526.
18. O'Farrell TJ, Murphy M, Alter J, Fals-Stewart W. Brief family treatment intervention to promote aftercare among substance abusing patients in inpatient detoxification: transferring a research intervention to clinical practice. *Addict Behav*. 2008;33:464–471. doi:S0306-4603(07)00296-1 [pii] /j.addbeh.2007.10.008.
19. Dunbar SB, Clark PC, Quinn C, Gary RA, Kaslow NJ. Family influences on heart failure self-care and outcomes. *J Cardiovasc Nurs*. 2008;23:258–265. https://doi.org/10.1097/01.JCN.0000305093.20012.b8.
20. Duhamel F, Dupuis F, Reidy M, Nadon N. A qualitative evaluation of a family nursing intervention. *Clin Nurse Spec*. 2007;21:43–49.
21. Dunbar SB, Clark PC, Deaton C, et al. Family education and support interventions in heart failure: a pilot study. *Nurs Res*. 2005;54:158–166. doi:00006199-200505000-00003 [pii].
22. Piette JD, Striplin D. A mobile health intervention supporting heart failure patients and their informal caregivers: a randomized comparative effectiveness trial. *J Med Internet Res*. 2015;17:e142. https://doi.org/10.2196/jmir.4550.
23. Fabbri M, Yost K, Finney Rutten LJ, et al. Health literacy and outcomes in patients with heart failure: a prospective community study. *Mayo Clin Proc*. 2018;93:9–15. https://doi.org/10.1016/j.mayocp.2017.09.018.
24. Kutner M, Greenberg EA, Jin Y, Paulsen C. *The Health Literacy of America's adults: Results from the 2003 National Assessment of Adult Literacy (nces 2006-483)*. Washington DC: National Center for Education Statistics; 2006.
25. Wu JR, Moser DK, Lennie TA, et al. Factors influencing medication adherence in patients with heart failure. *Heart Lung*. 2008;37:8–16. https://doi.org/10.1016/j.hrtlng.2007.02.003.
26. Evangelista LS, Rasmusson KD, Laramee AS, et al. Health literacy and the patient with heart failure–implications for patient care and research: a consensus statement of the Heart Failure Society of America. *J Card Fail*. 2010;16:9–16. https://doi.org/10.1016/j.cardfail.2009.10.026.
27. Kalichman SC, Pope H, White D, et al. Association between health literacy and HIV treatment adherence: further evidence from objectively measured medication adherence. *J Int Assoc Physicians AIDS Care*. 2008;7:317–323. https://doi.org/10.1177/1545109708328130.
28. Kripalani S, Gatti ME, Jacobson TA. Association of age, health literacy, and medication management strategies with cardiovascular medication adherence. *Patient Educ Couns*. 2010;81:177–181. https://doi.org/10.1016/j.pec.2010.04.030.
29. Williams MV, Davis T, Parker RM, Weiss BD. The role of health literacy in patient-physician communication. *Fam Med*. 2002;34:383–389.
30. Glanz K, Rimer BK, Viswanath K. *Health Behavior and Health education: Theory research and Practice*. San Francisco: Jossey-Bass; 2008.
31. Lee SY, Arozullah AM, Cho YI. Health literacy, social support, and health: a research agenda. *Soc Sci Med*. 2004;58:1309–1321. https://doi.org/10.1016/s0277-9536(03)00329-0.
32. Davis TC, Wolf MS, Bass 3rd PF, et al. Literacy and misunderstanding prescription drug labels. *Ann Intern Med*. 2006;145:887–894. https://doi.org/10.7326/0003-4819-145-12-200612190-00144.
33. Davis TC, Wolf MS, Bass 3rd PF, et al. Low literacy impairs comprehension of prescription drug warning labels. *J Gen Intern Med*. 2006;21:847–851. https://doi.org/10.1111/j.1525-1497.2006.00529.x.
34. Wu JR, Holmes GM, DeWalt DA, et al. Low literacy is associated with increased risk of hospitalization and death among individuals with heart failure. *J Gen Intern Med*. 2013;28:1174–1180. https://doi.org/10.1007/s11606-013-2394-4.
35. Wu JR, Frazier SK, Rayens MK, et al. Medication adherence, social support, and event-free survival in patients with heart failure. *Health Psychol*. 2013;32:637–646. https://doi.org/10.1037/a0028527.
36. Lora CM, Gordon EJ, Sharp LK, et al. Progression of CKD in Hispanics: potential roles of health literacy, acculturation, and social support. *Am J Kidney Dis*. 2011;58:282–290. https://doi.org/10.1053/j.ajkd.2011.05.004.
37. Wu JR, DeWalt DA, Baker DW, et al. A single-item self-report medication adherence question predicts hospitalisation and death in patients with heart failure. *J Clin Nurs*. 2014;23:2554–2564. https://doi.org/10.1111/jocn.12471.
38. DeWalt DA, Broucksou KA, Hawk V, et al. Comparison of a one-time educational intervention to a teach-to-goal educational intervention for self-management of heart failure: design of a randomized controlled trial. *BMC Health Serv Res*. 2009;9:99. https://doi.org/10.1186/1472-6963-9-99.
39. Wu JR, Moser DK, Chung ML, Lennie TA. Predictors of medication adherence using a multidimensional adherence model in patients with heart failure. *J Card Fail*. 2008;14:603–614. https://doi.org/10.1016/j.cardfail.2008.02.011.
40. Riegel B, Moser DK, Buck HG, et al. Self-care for the prevention and management of cardiovascular disease and stroke: a scientific statement for healthcare professionals from the american heart association. *J Am Heart Assoc*. 2017;6. https://doi.org/10.1161/jaha.117.006997.
41. Wu JR, Corley DJ, Lennie TA, Moser DK. Effect of a medication-taking behavior feedback theory-based intervention on outcomes in patients with heart failure. *J Card Fail*. 2012;18:1–9. https://doi.org/10.1016/j.cardfail.2011.09.006.
42. Hansberry DR, John A, John E, et al. A critical review of the readability of online patient education resources from radiologyinfo.Org. *AJR Am J Roentgenol*. 2014;202:566–575. https://doi.org/10.2214/ajr.13.11223.
43. Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. *Med Care*. 1986;24:67–74.
44. Park LG, Howie-Esquivel J, Dracup K. Electronic measurement of medication adherence. *West J Nurs Res*. 2015;37:28–49. https://doi.org/10.1177/0193945914524492.
45. Dobbels F, De Geest S, van Cleemput J, Droogne W, Vanhaecke J. Effect of late medication non-compliance on outcome after heart transplantation: a 5-year follow-up. *J Heart Lung Transplant*. 2004;23:1245–1251. https://doi.org/10.1016/j.healun.2003.09.016.
46. Wu JR, Chung M, Lennie TA, Hall LA, Moser DK. Testing the psychometric properties of the medication adherence scale in patients with heart failure. *Heart Lung*. 2008;37:334–343. https://doi.org/10.1016/j.hrtlng.2007.10.001.
47. Dunbar SB, Clark PC, Stamp KD, et al. Family partnership and education interventions to reduce dietary sodium by patients with heart failure differ by family functioning. *Heart Lung*. 2016;45:311–318. https://doi.org/10.1016/j.hrtlng.2016.04.001.
48. Stamp KD, Dunbar SB, Clark PC, et al. Family partner intervention influences self-care confidence and treatment self-regulation in patients with heart failure. *Eur J Cardiovasc Nurs*. 2016;15:317–327. https://doi.org/10.1177/1474515115572047.
49. Canty-Mitchell J, Zimet GD. Psychometric properties of the multidimensional scale of perceived social support in urban adolescents. *Am J Commun Psychol*. 2000;28:391–400. https://doi.org/10.1023/A:1005109522457.
50. Picardi A, Mazzotti E, Gaetano P, et al. Stress, social support, emotional regulation, and exacerbation of diffuse plaque psoriasis. *Psychosomatics*. 2005;46:556–564. https://doi.org/10.1176/appi.psy.46.6.556.
51. Gallagher BD, Muntner P, Moise N, Lin JJ, Kronish IM. Are two commonly used self-report questionnaires useful for identifying antihypertensive medication nonadherence? *J Hypertens*. 2015;33:1108–1113. https://doi.org/10.1097/hjh.0000000000000503.
52. Kessler JB, Troxel AB, Asch DA, et al. Partners and alerts in medication adherence: a randomized clinical trial. *J Gen Intern Med*. 2018. https://doi.org/10.1007/s11606-018-4389-7.
53. Ruppar TM, Delgado JM, Temple J. Medication adherence interventions for heart failure patients: a meta-analysis. *Eur J Cardiovasc Nurs*. 2015. https://doi.org/10.1177/1474515115571213.
54. Murray MD, Young J, Hoke S, et al. Pharmacist intervention to improve medication adherence in heart failure: a randomized trial. *Ann Intern Med*. 2007;146:714–725. https://doi.org/10.7326/0003-4819-146-10-200705150-00005.