

ORIGINAL ARTICLE

The effects of laughter therapy on depression symptoms in patients undergoing center hemodialysis: A pragmatic randomized controlled trial

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Abstract

Introduction: People with end-stage renal disease undergoing hemodialysis are at increased risk for stress, anxiety, and depression. The study objective was to measure the effect of intradialytic group laughter therapy on depressive symptoms in people on hemodialysis (HD).

Methods: Pragmatic randomized controlled trial conducted with prevalent HD patients in 10 centers in Northern California. The intervention group received a once weekly, 30-minute group laughter therapy session for 8 weeks. Primary outcome was the number of people with depressive symptoms as measured using the four item Patient Health Questionnaire. Secondary outcomes were anxiety, subjective well-being, and patient-reported outcome measures.

Findings: In all, 151 participants completed both predepression and postdepression symptom measures (72 intervention and 79 control). The proportion of patients with self-reported depressive symptoms changed from 17 (22%) to 16 (20%), in the control and from 11 (17%) to 5 (8%) in the intervention arms, respectively ($P = 0.04$). In the control arm, 7 out of the 17 patients with self-reported depressive symptoms at baseline continued to report depressive symptoms at follow up compared to the intervention arm where only 1 of 12 patients continued to report depressive symptoms. No differences were noted between the groups for reported anxiety, patient-reported dialysis symptoms, and subjective well-being.

Discussion: This study found intradialytic group laughter can decrease the number of people with depressive symptoms receiving hemodialysis. Larger and long-term studies are required to evaluate the effect of intradialytic laughter on patient related outcomes and quality of life.

Keywords: Hemodialysis, laughter, anxiety, depression, anxiety, end-stage kidney disease

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INTRODUCTION

End-stage renal disease (ESRD) is associated with increased stress, anxiety, and depression.^{1,2} These psychological stresses are particularly heightened in patients when commencing dialysis^{3,4} continuing throughout their dialysis experience.⁵ Depression prevalence estimates in

ESRD vary widely, with a recent meta-analysis of 249 studies concluding that the prevalence of depressive symptoms for ESRD using self or clinician-administered tools was 39.3%.⁶

Psychological stresses have a significant impact on physical health, social impact, quality of life, and mortality in dialysis.^{1,7} Depression is associated with a significant increase in mortality,⁷ inflammation,⁸ increased post dialysis recovery time,⁹ inactivity,¹⁰ nonadherence to physician orders, medications, fluid control, recommended diet, and dialysis treatments and significantly impacts the relationship with health care professionals and other patients.^{11,12}

The choice of pharmacological or nonpharmacological treatments for depression is complex for people with ESRD. A recent trial comparing sertraline, a selective serotonin reuptake inhibitor (SSRI), with cognitive behavioral therapy (CBT) found lower depression symptom scores for SSRIs, however, SSRIs were associated with greater adverse events than CBT.¹³ For some dialysis patients, nonpharmacological treatments are preferable to antidepressant SSRIs given their already high pill burden and treatment preferences.¹⁴ Nonpharmacological treatments include therapies such as CBT,¹⁵ meditation,¹⁶ exercise,¹⁷ acupuncture,¹⁸ quality of life therapy (QOLT),¹⁹ painting and drawing therapy,^{20,21} mindfulness-based art therapy,²² music therapy,²³⁻²⁵ web-based interventions,²⁶ and laughter therapy.²⁷ From the nonpharmacological interventions, CBT is the only nonpharmacological intervention tested in suitably powered randomized trials.

Laughter therapy consists of “intentional laughter” practiced over a sustained period to enhance the many benefits associated with laughter. In nondialysis settings, laughter therapy has been associated with significant improvements in quality of life.^{28,29} In specific chronic disease conditions, laughter therapy has provided respite from adverse effects associated with illness by improving mood,³⁰ decreasing pain³¹ and depression.³² In the dialysis context, small noncontrolled studies have shown associations with improved mood and subjective well-being,^{27,33} however, randomized studies have not been reported.

We previously demonstrated in a mixed methods pilot study, the feasibility, safety, and acceptance of laughter therapy with over 70% of staff and patients agreeing that laughter had a positive impact on patient mood and recommended laughter therapy in dialysis centers.³⁴ The study reported here, to be termed laugh-out-loud hemodialysis study (LOL-HD), aimed to test the hypothesis that intradialytic group laughter therapy would have a beneficial effect on the primary measure of interest: depressive symptoms. Secondary measures were anxiety, subjective well-being, and symptom-related patient-reported outcome measures (PROMs).

MATERIALS AND METHODS

Study overview

This study was a pragmatic randomized control clinical trial in which dialysis centers were randomized to an eight session, once-per-week, 30-minute group laughter therapy while receiving dialysis or usual care.

Inclusion/exclusion criteria

Participants were identified as prevalent patients receiving hemodialysis in 10 hemodialysis centers in California operated by a nonprofit dialysis organization. Thirty-five Northern Californian centers were asked to express interest with 10 centers volunteering. In these 10 centers, all adults over the age of 18 years, and able to understand English in order to complete the 18-item pre and post survey, and with no cognitive impairment, were eligible for inclusion. The final sample studied were those participants who completed pre and post surveys.

Randomization

Randomization was performed on a center basis as a 1:1 ratio, via a computer generated randomization function by an external research assistant (RA) who was not involved in LOL-HD study. Randomization was performed on a center basis because the laughter intervention was a group intervention making it impractical to provide the intervention individually. Allocation concealment was assured by not providing the randomized sequence to the centers until they agreed to participate. The randomization allocation was provided to the LOL-HD RA who assigned centers to their prerandomized study arm. This process ensured the complete separation of those involved with generation and allocation concealment from those involved in the implementation of allocating assignments. Following randomization allocation, participant and clinician blinding were not possible due to the nature of the laughter intervention.

Study procedures

Control group

Hemodialysis patients who were in the centers assigned to the usual care group were provided with standard hemodialysis care and no laughter intervention. Patients were given information sheets explaining laughter therapy; however, no discussion of the potential effects of

the laughter intervention was provided in the information sheets.

Laughter intervention group

Staff were provided education in the laughter intervention centers consisting of one 30-minute education session, and one short laughter therapy practical demonstration. (Video link can be found at <http://www.satellitehealth.com/video-center/hemodialysis/laugh-out-loud-hemodialysis.aspx>.) Laughter therapy sessions were performed once weekly at mutually agreed times, approximately 1 hour after patients commenced their hemodialysis treatment. Each 30-minute session consisted of: breathing and stretching exercises; facilitated intentional laughter exercises; and finished with laughter meditation. Patients whose first language was not English were given a 10-minute information explanation by a staff member fluent in the patient's preferred language. This enabled non-English patients to participate in the laughter sessions, so they would not feel left out because of a lack of understanding of the laughter intervention. This was necessary because this was a group delivered intervention in an open hemodialysis center where individuals participating could not be placed in separate rooms. These non-English speaking individuals were not included in the sample numbers because they were unable to complete the English language survey measures.

The interventions were based on our pilot study and described in detail in two previous publications.^{27,34} Weekly sessions were administered by at least two Certified Laughter Yoga Leaders. These Laughter Yoga leaders' training and qualifications are administered by Laughter Yoga University and Laughter Wellness Institute^{35,36} and their designated affiliates. The basic qualification is a Certified Laughter Yoga Leader, with higher qualifications as a Certified Laughter Yoga Teacher, Certified Laughter Yoga Master Trainer, and Diploma in Laughter Wellness.

Each clinic had a designated local laughter study representative assigned whose main responsibility was to liaise between the center and the Laughter Therapists. The on-site representatives were either patient care technicians, registered nurses, dietitians, or social workers. Staff were encouraged to participate in the laughter therapy sessions during each 30-minute session. Allied health staff such as social workers and dietitians assisted by organizing their patient appointments around the prearranged laughter therapy session times. Nephrologists also assisted ensuring that patient care rounds were not scheduled during laughter therapy. Where possible, staff assisted the laughter therapists in engaging and encouraging patients.

Data collection

Data for the laughter therapy group were collected through paper-based questionnaires immediately before the first laughter therapy session and the hemodialysis session following the final laughter therapy session. Participants completed the surveys during the first hour of their hemodialysis treatment. Questionnaires for the control group were completed within 2 days of the time when the laughter therapy was started or ended at the randomized sites.

Study outcome measures

Primary outcome: The primary outcome of the study was change in the number of people with depressive symptoms in the laughter intervention group compared to the change in the control group, as measured by the depressive symptom subscale in the Patient Health Questionnaire (PHQ-4).³⁷ A score of 3 or greater for PHQ-4 depression subscale is considered valid for detecting depressive symptoms.

Secondary measures: Anxiety as measured using the anxiety sub-scale of the PHQ-4. A score of 3 or greater for the anxiety subscale is considered valid for detecting self-reported anxiety.³⁷ Subjective well-being, a measure for the construct of long term happiness, was measured using the Personal Wellbeing Index (PWI) a seven-item validated scale that rates satisfaction with life in seven domains: standard of living, health, achievements in life, relationships, safety, community, and future security, on an 11-point scale.³⁸ The scale has also established good psychometric properties in end stage kidney disease patients and other chronic diseases.^{39,40} PROMs using the London Evaluation of Illness (LEVIL) instrument.⁴¹ LEVIL is a six-item visual analogue scale (VAS) developed and used in hemodialysis patients to measure general well-being (GWB), pain, sleep, breathing, energy, and appetite.⁴² The anchors for GWB, sleep and appetite were "very poor"—"excellent," for pain and breathing "extreme"—"no problem," and for energy "extremely fatigued"—"full of energy." For each domain, the VAS allowed free selection of status along a line from worst (0) to best (100).⁴¹

The PHQ-4, PWI, and LEVIL scales added up to a combined 18-item questionnaire. Experience from previous questionnaire research has demonstrated dialysis patient survey burden when dialysis patients were asked greater than 20 questions.⁴³ In order to limit participant survey burden, we limited the survey to 18 questions to maximize patient questionnaire completion.

Statistical methods

A Cochran–Mantel–Haenszel (CMH) one-tailed test was used to determine whether the relative depressive symptoms were significantly lower for patients in the LOL group than the control group after controlling for baseline status. To examine the magnitude of the effects of this laughter intervention on reducing depressive symptoms, logistic regression was used to examine the odds ratio of having depressive symptoms, controlling for baseline status. The same tests were applied to anxiety measures. The secondary outcomes for the study were analyzed using repeated measures ANOVA with within-subjects factor time of measurement and between subjects factor treatment group.

The minimum sample size required for CMH test and logistic regression were calculated by using PASS software (PASS 2019 NCSS, LLC, Kaysville, UT, USA). We estimated the minimum sample size required, based on the different values of the prevalence of depression and varied expected effects of LOL on depression in patients on dialysis. Using CMH tests and assuming 30% baseline prevalence of depression, we found that the minimum sample size was 56 in each arm in order to achieve 80% power to reject the odds ratio set by the null hypothesis of 1.000 when the odds ratio is actually 0.250 (equivalent to reduction from 30% to 10%). The significance level of the test was set at 0.050. We then tested the sample size for general logistic regression where we determined that a logistic regression of a binary response variable on a binary independent variable with a sample size of 169 observations (of which 50% are in the group $X = 0$ and 50% are in the group $X = 1$) achieved 80% power at a 0.050 significance level to detect a change in $\text{Prob}(Y = 1)$ from the baseline value of 0.250 to 0.100. This change corresponds to an odds ratio of 0.333. A one-sided Wald test was used. Data from participants who completed both pre and post survey were included in the analysis. We sought to include an intraclass coefficient (ICC) on completion of data collection.

Ethical approval was granted by SALUS Independent Review Board # SR065LOL in March 2018. Study recruitment was performed during April and May 2018 with interventions running from May 2018 to September 2018. Procedures followed were in accord with the ethical standards of the committee on human experimentation in accord with the Declaration of Helsinki and its revisions. Waiver of consent was approved based on the following waiver criteria: (a) the laughter intervention was low risk and (b) the consent process would critically bias subject participation. The trial was registered at ClinicalTrials.gov (identifier: NCT04098627). CONSORT

statement for improving the reporting of pragmatic trials was addressed (Supplementary Table 1).⁴⁴

RESULTS

From 10 hemodialysis centers, 270 participants completed the pre survey. From these, 151 participants completed the post surveys, 72 in the laughter intervention group, and 79 in the control group (Figure 1). The mean cluster size in the intervention group was 14.4 (SD 1.14) and in the control group was 15.8 (SD 4.6).

The percentage of patients who reported depressive symptoms decreased from 17 (22%) to 16 (20%) in the control group and 11 (17%) to 5 (8%) in the laughter intervention group (Table 1). In the control group, of the 17 patients who reported depressive symptoms at baseline, 7 reported depressive symptoms at follow-up. In the intervention group, only 1 out of the 11 patients who reported depressive symptoms at baseline also reported depressive symptoms at follow-up ($P = 0.04$). Adjusting for baseline depression status, there was an odds ratio of 0.37 (95% CI: 0.13–1.01, $P = 0.05$) for depressive symptoms reported in the intervention arm as compared to the control arm.

There was no difference in change in anxiety symptoms between the two groups (Table 2). Two out of 11 patients in the control group continued to report anxiety symptoms, while 2 out of 4 patients in the laughter intervention group remained reporting anxiety symptoms. The odds ratio between the treatment group and the control group was 0.64 (95% CI: 0.20–2.10, $P = 0.46$).

No treatment effect was found for the PROMs using the LEVIL instrument, or subjective well-being using the PWI instrument (Tables 3 and 4). No serious adverse events were reported related to the study.

DISCUSSION

In this pragmatic randomized controlled trial (RCT), we developed and implemented an intradialytic laughter therapy program. We compared 8 weeks of 30 minute, once-per-week group intradialytic laughter therapy with a control group who received usual care. We demonstrated that laughter therapy can decrease the number of dialysis patients with depressive symptoms compared to a control group. Our study provides stronger evidence than previous smaller hemodialysis noncontrolled studies^{27,33,34} supporting an association between laughter therapy and an improvement in patient-reported depressive symptoms and mood. Previous randomized studies in people with depression showed similar improvements

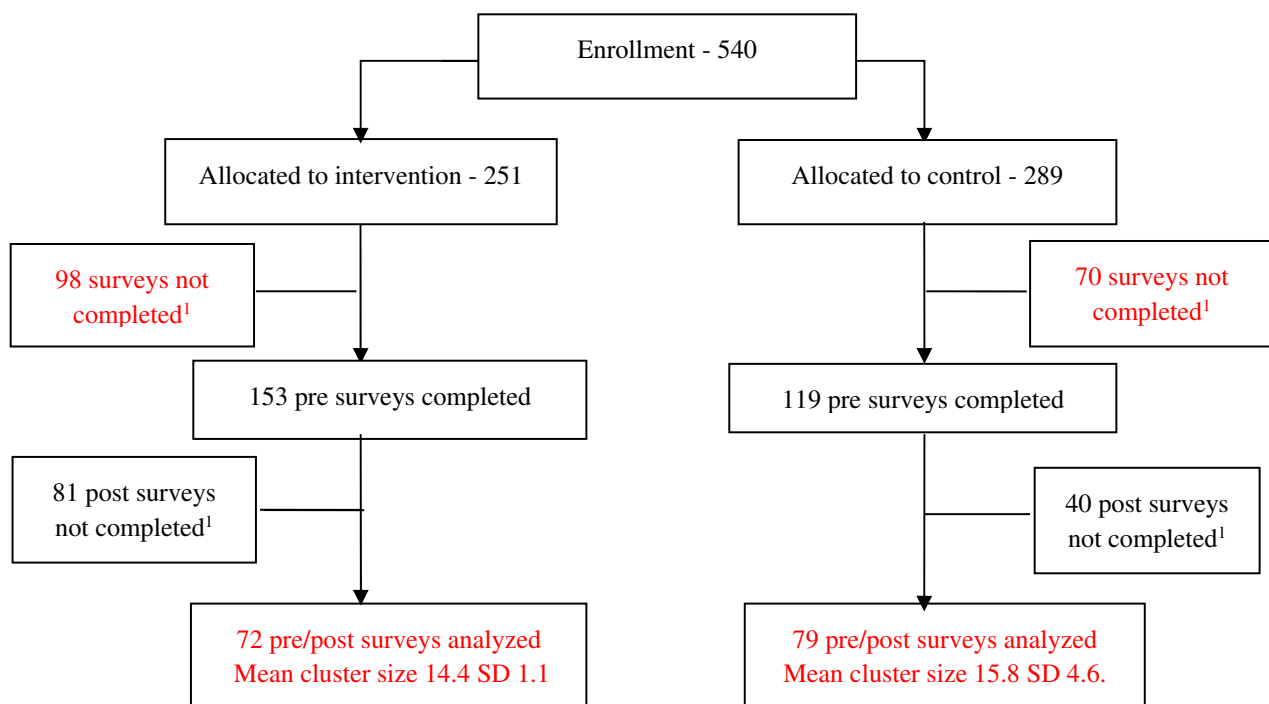


Figure 1 Laughter study participant flow diagram. Superscript 1 indicates reasons for noncompletion not recorded. SD = standard deviation. [Color figure can be viewed at wileyonlinelibrary.com]

Table 1 Proportion of participants with reported depression using PHQ-4 (P = 0.04)

Group	Period	Depression symptom reports	N
Control	Baseline	17 (22%)	79
	Follow-up without intervention	16 (20%)	
Treatment	Baseline	11 (17%)	72
	Follow-up after intervention	5 (8%)	

in depression using the Depression Anxiety Scale Stress Score⁴⁵ and the Geriatric Depression Scale.³² A non-controlled healthy sample also described the reduced anxiety effects of laughter, as measured by the Profile of Mood States-Brief Japanese Version.⁴⁶

Depression is a major ESRD comorbidity with 23% of patients suffering depressive symptoms⁶ and reporting lower levels of happiness than age-matched nondialysis

cohorts.⁴⁰ Therefore, interventions such as laughter therapy may have a place in hemodialysis centers. The success of laughter may be associated with the potential for laughter therapy to improve interpersonal interaction, relationships, increasing helpfulness and building group identity, solidarity, and cohesiveness. Intentional laughter has been shown to foster improved communication within teams that leads to a less confrontational approach

Table 2 Proportion of participants with reported anxiety using PHQ-4

Group	Period	Anxiety symptom reports	N
Control	Baseline	11 (14%)	79
	Follow-up without intervention	9 (11%)	
Treatment	Baseline	4 (6%)	72
	Follow-up after intervention	5 (7%)	

Table 3 Patient reported outcome changes: intervention and control

	Control		Intervention		P value
	$\bar{x}$	SD	$\bar{x}$	SD	
General well-being pre	76.8	22.7	74.5	25.8	0.86
General well-being post	75.9	23.3	77.0	21.9	
Post - pre	-0.9	23.9	2.4	28.3	
Bodily pain pre	74.3	28.8	74.0	32.2	0.62
Bodily pain post	71.2	31.2	75.7	30.0	
Post - pre	-3.1	37.4	1.7	33.0	
Feeling drained pre	59.8	28.7	53.6	33.1	0.56
Feeling drained post	61.6	29.1	63.0	27.5	
Post - pre	1.8	30.6	9.4	33.4	
Sleep quality pre	70.5	28.8	62.5	35.3	0.47
Sleep quality post	61.6	29.9	62.9	34.2	
Post - pre	-8.9	33.3	0.3	31.7	
Difficulty breathing pre	86.7	20.4	84.5	26.3	0.68
Difficulty breathing post	76.4	27.4	81.6	28.6	
Post - pre	-10.3	27.6	-2.9	27.5	
Appetite pre	76.5	28.7	71.2	30.2	0.28
Appetite post	76.6	23.3	73.1	30.7	
Post - pre	0.0	24.4	1.9	31.4	

Post = measure taken the treatment following the final laughter session and the matched day in the control group; Pre = measure taken dialysis treatment prior to commencing laughter in the intervention and the matched day in control group; SD = standard deviation; $\bar{x}$ = mean.

in tense situations and a change from individual competitiveness to team cooperation.⁴⁷ These effects may have application for the hemodialysis context where stress is increased.

Laughter therapy has been used widely for people with chronic disease, mental health conditions, and cancer.⁴⁸ Although our study was not powered to measure the effect of patient reported outcomes and subjective well-being, laughter therapy can have both psychological and physical effects through exercising the facial, chest, abdominal, and skeletal muscles.⁴⁰ Furthermore, laughter therapy has been associated with improvements in cardiovascular function, respiratory function, elevate pain tolerance, and increased immunity.⁴⁹ No previously published studies have tested these effects in ESRD patients.

The pragmatic aspects of conducting a laughter therapy RCT in hemodialysis centers are significant. The decision to waiver formal written consent had advantages and disadvantages. The advantages were that we potentially obtained a less biased sample, because the expectation was that patients may refuse if they were asked for formal consent, however, once they understood the laughter intervention better they may decide to participate. The disadvantage was that under strict independent review board conditions, we did not promote the evidence-based research supporting the laughter therapy to ensure that any effect was the laughter therapy itself.

Furthermore, we did not collect and analyze patient level demographic clinical and demographic data in keeping with our conditions for waiver of consent.

Introducing any intradialytic group activity to hemodialysis patients was challenging due to patients' intradialytic routines that include watching television and listening to music. Overcoming this challenge was assisted by the learnings of our previous noncontrolled pilot study held in two Northern Californian hemodialysis centers.³⁴ Strategies to increase laughter therapy acceptance included staff and patient education, laughter therapist education, laughter therapist discussions with patients prior to the intervention, staff laughter therapy sessions, and encouraging staff involvement in patient sessions. Even with these strategies, we still found that approximately 20% of dialysis patients were still reluctant to participate. These strategies and study results are likely to be generalizable and transferrable across hemodialysis centers in the United States.

To implement laughter therapy is a major undertaking for a hemodialysis center, and thus a recognized change management or quality improvement approach should be considered. The study team has developed web-based tools and examples of laughter therapy exercises that trained laughter therapists can use in intradialytic laughter therapy.⁵⁰ Patient engagement will assist in this process and ideally, a patient or family member may train as

Table 4 Subjective well-being changes: intervention and control groups

	Control		Intervention		P value
	$\bar{x}$	SD	$\bar{x}$	SD	
Standard of living pre	7.9	2.5	7.8	2.7	0.96
Standard of living post	7.9	2.4	7.9	2.5	
Post - pre	0.0	2.8	0.1	3.3	
Health pre	7.0	2.5	6.6	2.8	
Health post	7.0	2.3	6.8	2.6	0.36
Post - pre	-0.0	2.7	0.1	2.9	
Achieving pre	7.1	2.8	7.2	2.8	
Achieving post	7.3	2.3	7.6	2.4	
Post - pre	0.1	2.5	0.5	3.4	0.57
Relationships pre	8.3	2.4	8.4	2.6	
Relationships post	8.3	2.2	8.5	2.3	
Post - pre	-0.0	2.2	0.1	2.8	
Safety pre	9.0	1.6	8.7	2.3	0.82
Safety post	8.7	1.9	8.9	1.9	
Post - pre	-0.3	1.6	0.2	2.7	
Community pre	7.4	2.8	7.3	3.4	
Community post	7.3	3.0	7.4	2.9	0.85
Post - pre	-0.1	2.6	0.2	4.1	
Security pre	7.8	2.5	7.9	2.8	
Security post	7.9	2.6	8.0	2.6	
Post - pre	0.1	2.6	0.2	3.3	0.81
Well-being pre	7.8	1.8	7.7	2.1	
Well-being post	7.8	1.8	7.9	1.9	
Post - pre	-0.0	1.6	0.2	2.2	

Post = measure taken the treatment following the final laughter session and the matched day in the control group; Pre = measure taken dialysis treatment prior to commencing laughter in the intervention and the matched day in control group; SD = standard deviation; $\bar{x}$ = mean.

a laughter therapy leader. In addition, timing of the laughter for a hemodialysis center is important as commencing during a major health crisis or pandemic may be positive and is yet to be explored. Costs are limited to the laughter therapist charges and there are no consumables or capital expenses required.

This study has both strengths and limitations. The major strength is that this is the first and the largest RCT designed intradialytic group laughter intervention study. The pragmatic design highlighted the logistic challenges of an RCT using a group laughter intervention and lessons learned for future studies. We recognize certain limitations of the study. First, the scoring used in the PHQ-4 denotes a screening tool for identifying depressive and anxiety symptoms, and is not a diagnostic tool. PHQ-4 has been used as a standardized test in interventional studies and is a valid indicator for status of change resulting from an intervention.³⁷ Given the waiver of consent Institutional Review Board condition, patients did not consent to provide demographic or clinical data.

Hence, we were unable to analyze any baseline differences between control and intervention samples and we were unable to adjust for gender, other depressive or comorbid conditions or socioeconomic status variables. Fifty-six percent completing both pre and post surveys (44% did not complete post survey) which may have introduced bias to our results. The intention to include an ICC was not conducted because of low participants in each cluster; however, we recognize a very small possibility that the low ICC could alter the findings. Therefore, we did not include the HD centers as a factor in the ANOVA analysis due to the fact that for each of the centers, insufficient observations were collected (less than specified in the sample size calculations for the study).

In summary, this study demonstrated that laughter therapy can reduce depressive symptoms in a hemodialysis cohort. Laughter is a safe group therapy that could be added to hemodialysis programs as one strategy to improve the patient's dialysis experience. Laughter therapy can sit alongside other possible complementary

treatments such as meditation, music therapy, art therapy, and technologies such as gaming and virtual reality to improve the patient's dialysis experience. While these kinds of interventions or services are not part of dialysis delivery care models at this time, consideration of such "out of the box" interventions could benefit the patient dialysis experience, mental health, GWB, and quality of life, and build a healthier, happier in-center dialysis culture.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Supplementary Table 1 Checklist of items for reporting pragmatic trials