DATA ANALYSIS PLAN: Meditation and Stretching Study

Study No. ClinicalTrials.gov #	6927 NCT02344537	Study name	Meditation and Stretching for Post Treatment Lyme Disease Syndrome
Date of plan Date of revision	11/4/19 11/24/21	Chief investigator	Brian Fallon
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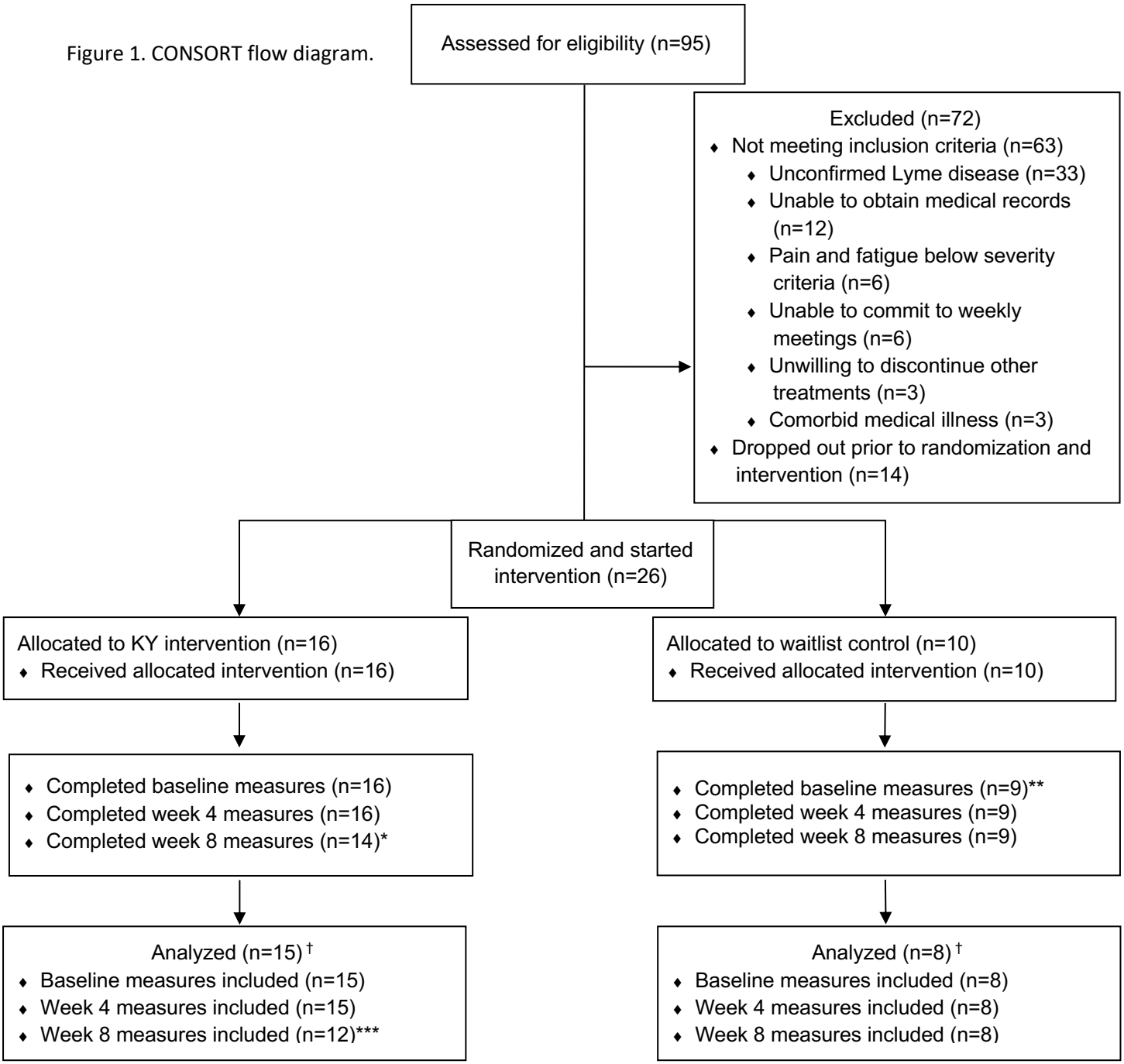
Background to the study and analysis			
Alternative treatments for PTLDS that can assuage fatigue, muscle and joint pains, and improve cognitive function are urgently needed. Recent studies indicate that meditation can be a helpful strategy in reducing muscle pain and improving energy among patients with other chronic musculoskeletal disorders, such as fibromyalgia. We wish to conduct a preliminary study to examine the efficacy of meditation among patients with PTLDS and CLD. We plan to assess the degree in which this practice can reduce Post-Treatment Lyme Disease and Chronic Lyme Disease symptoms. Because fatigue and pain are so common among patients with PTLDS or CLD, the primary focus of this study will be fatigue and pain. Secondary outcomes will include cognitive complaints, physical and mental functioning, medical utilization, somatic symptoms, and psychopathology.			
Number study participants	26	Duration of study	8 weeks
Study research question	The proposed study seeks to evaluate the efficacy of meditation among patients previously treated for Lyme disease but continuing to experience prominent symptoms of fatigue and/or pain.		
Specific hypotheses under study	• [Primary outcome]. People who receive treatment will self-report greater change in core symptoms of fatigue and pain and perceived global health at end of KY treatment phase than people who are randomized to the wait-list. • [Secondary outcome]. People who receive treatment will self-report greater change in physical & social functioning, sleep, cognitive functioning, mindfulness, multisystemic symptoms, pain interference, anxiety, and depression at end of Kundalini yoga treatment phase than people randomized to the wait-list. • To assess the compliance of patients with weekly group meditation/stretching therapy and (based on self-report) the daily meditation therapy. • To assess whether the pre-treatment measures of stress, trauma history, illness perception, intolerance of uncertainty, and pain catastrophizing are variables that are related to 8 week outcomes		
Endpoints or outcomes of interest	Establish feasibility for meditation as an alternative treatment for fatigue and pain in PTLDS		

Data details	
Study type	Longitudinal treatment study
Data sets used	Columbia University

Analysis package	R
Study population	Post-treatment Lyme disease patients
Inclusion/exclusion criteria for participants	Broad
Predictor variables	Treatment arm
Main analysis: Primary outcome measures	Pain VAS, PROMIS Fatigue, PROMIS Pain Interference, Perceived Global Health
Main analysis: Secondary outcome measures	General Symptom Questionnaire-30, PROMIS anxiety, PROMIS depression, PROMIS Sleep Disturbance, PROMIS Physical Function PROMIS Ability to Participate in Social Roles and Activities, Beck Depression, NeuroQoL Applied Cognition General Concerns, Mindful Attention Scale
Secondary analysis: Primary outcome measures	Pain and fatigue at 8 weeks.
Covariates	Uncertainty Scale Short Form; catastrophizing subscale of the Coping Strategies Questionnaire; Trauma History Screen; Perceived Stress Scale; Whiteley Index; Brief Illness Perception Questionnaire
Sub-groups	N/A
Approach to dealing with missing data	Longitudinal mixed models estimate parameters based on means. Imputation/deletion is not needed for these analyses. Pairwise deletion for regression models should be considered. Given the very small sample, imputation may distort results.

Proposed analytical strategy
* Descriptive characteristics of study sample are presented in a table Longitudinal mixed models conducted on primary outcome measures: (1) PROMIS Pain (2) PROMIS Fatigue (3) PROMIS Pain Inference, and (4) Satisfaction with Global Health with study arm, time (baseline, 4-week, 8-week), and the interaction term (between the main predictor “group” and time) included. Intercepts for every subject modelled as random effects. Longitudinal mixed models conducted on secondary outcome measures with study arm, time (baseline, 4-week, 8-week), and the interaction term (between the main predictor “group” and time) included. Intercepts for every subject modelled as random effects. Adherence is reported as percent of participants who attended weekly group sessions and if possible, as means and standard deviations for group attendance and daily practice.

Figure 1. CONSORT flow diagram.



**2 participants did not complete their week 8 questionnaires, although both completed all 8 weeks of the KY intervention.*

***Data was lost for 1 participant*

****1 participant started a concomitant treatment at week 6 of the study; their week 8 data were excluded.*

†*2 participants removed from dataset (1 from KY intervention, 1 from waitlist) due to mistaken enrollment (age >65)*

Table 1. Demographics and clinical characteristics of participants who received allocated intervention

	KY (n = 15)	WLC (n = 8)	Overall (n = 23)
Sex = Male (n (%))	7 (46.7)	4 (50.0)	11 (47.8)
Ethnicity (n (%))			
Hispanic	1 (6.7)	0 (0.0)	1 (4.3)
White (non-Hispanic)	12 (80.0)	6 (75.0)	18 (78.3)
Not reported	2 (13.3)	2 (25.0)	4 (17.4)
Age (M (SD))	48.47 (12.99)	62.62 (14.51)	53.39 (14.90)
Marital Status (n (%))			
Single (never married)	1 (6.7)	2 (25.0)	3 (13.0)
Married/Living with partner	11 (73.3)	5 (62.5)	16 (69.6)
Divorced/Separated	1 (6.7)	0 (0.0)	1 (4.3)
Not reported	2 (13.3)	1 (12.5)	3 (13.0)
Education (n (%))			
Completed high school or GED	2 (13.3)	0 (0.0)	2 (8.7)
Some college (less than 4 years)	4 (26.7)	1 (12.5)	5 (21.7)
Completed 4-year college degree	2 (13.3)	3 (37.5)	5 (21.7)
Completed post-college degree	4 (26.7)	2 (25.0)	6 (26.1)
Not reported	3 (20.0)	2 (25.0)	5 (21.7)
Employment (n (%))			
Employed at least half-time for pay	1 (6.7)	0 (0.0)	1 (4.3)
Employed full-time for pay	2 (13.3)	4 (50.0)	6 (40.0)
Unemployed more than 6 months	4 (26.7)	0 (0.0)	4 (17.4)
Disabled	4 (26.7)	0 (0.0)	4 (17.4)
Retired	0 (0.0)	1 (12.5)	1 (4.3)
Other	1 (6.7)	2 (25.0)	3 (13.0)
Not reported	3 (20.0)	1 (12.5)	4 (17.4)
Medical Utilization (n (%))*			
Lifetime: medical hospitalization	11 (78.6)	6 (75.0)	17 (77.3)
Lifetime: psychiatric hospitalization	3 (21.4)	0 (0.0)	3 (13.6)
Lifetime: major surgery	11 (78.6)	6 (75.0)	17 (77.3)
Past 3 months: emergency room visit	1 (7.1)	0 (0.0)	1 (4.5)
Past 3 months: urgent care visit	2 (14.3)	1 (12.5)	3 (13.6)
Past 3 months: overnight hospitalization	1 (7.1)	0 (0.0)	1 (4.5)

*1 KY participant did not complete medical utilization questions