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REGULAR ARTICLE

The Effects of Aerobic Exercise on Psychological Functioning in Family Caregivers: Secondary Analyses of a Randomized Controlled Trial

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Abstract

Background The responsibility and stress of being a family caregiver are associated with reduced physical and mental health.

Purpose To examine whether a 24-week aerobic exercise program improves multiple aspects of psychological functioning in family caregivers.

Methods Family caregivers of patients with Alzheimer's disease and other dementias (n = 68) were recruited and randomized into either an aerobic exercise group (n = 34) or a waitlist control group (n = 34). The exercise group was assigned a 24-week aerobic training program that incrementally increased the intensity, duration, and frequency of the exercise program until 150 min of moderate to vigorous activity were completed per week by the ninth week. Twelve measures of psychological functioning were administered at baseline and compared with responses completed following the intervention.

Results Multilevel modeling revealed significant decreases in caregiver burden (β = −4.60, 95% confidence interval [CI] = [−8.82, −0.38], RLMM2 = 0.11) and depression (β = −2.59, 95% CI = [−4.79, −0.38], RLMM2 = 0.13), as well as increases in mastery (β = 1.78, 95% CI = [0.09, 3.46], RLMM2 = .04) in the exercise intervention group compared to the control group.

Conclusion Family caregivers report high levels of depression and caregiver burden. Engagement in a 24-week exercise intervention can ameliorate the perceived burden of caregiving, symptoms of depression, and their sense of mastery.

Keywords: Caregivers · Burden · Depression · Mastery · Physical activity · Intervention

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Introduction

The population of the USA is aging, with the percentage of the population over 65 years of age set to increase from 13.7% in 2012 to 20.9% by 2050 [1]. With an aging population comes an increased need for caregivers, particularly as the number of adults with age-related neurodegenerative diseases (e.g., Alzheimer's disease) rise [2]. As the high cost of professional caregiving can be prohibitive, informal family caregivers are assuming this role in increasing numbers [3]. In 2015, over 34 million Americans provided unpaid care to an older adult [4].

Informal caregiving is associated with an approximately 60% higher risk of developing cardiovascular disease [5] and a similar risk of early mortality [6]. These effects are especially pronounced when providing more than 9 hr of care per week to a family member with dementia [7]. Providing care to a family member with a dementia-related condition is known to be emotionally taxing and can result in higher risk of mental health conditions, including depression [8]. Caregiving,

though, is not merely detrimental to mental and physical health in terms of diagnosable disorders. Caregivers, and especially caregivers of family members with a dementia-related condition, report poorer psychological functioning in general, including greater chronic psychological stress and lower general subjective well-being compared to noncaregivers [9]. A recent cross-sectional study has further identified lower levels of social support and perceptions of self-mastery among family caregivers compared to noncaregivers [10].

The primary focus of interventions to improve psychological functioning of caregivers and reduce caregiver burden have historically been psychosocial in their nature [11, 12]. However, there is evidence to suggest that exercise may improve caregivers' psychological functioning. In the general population, regular physical activity is associated with improvements in a range of outcomes, including delayed cognitive decline [13], reduced depressive symptomatology [14], and reduced risk of early mortality [15]. A systematic review examining the association between physical activity and caregivers' psychological functioning found that physical activity was associated with lower levels of subjective distress and increased levels of perceived quality of life and well-being [16]. Approximately half of the reviewed studies found improvements from any type of physical activity intervention (e.g., aerobic exercise and yoga) in at least one measure of psychological health, including depressive symptomatology, distress, chronic stress, anxiety, and general well-being. In one study [17] reported in the systematic review [16] that investigated anger, no changes were observed following the intervention. The review also reported significant improvements in caregiver burden, and one study [18] found a significant increase in participants' self-efficacy for exercising but not for self-care. No evidence for changes in adaptive coping strategies was found in the systematic review, nor were there significant changes in reported levels of social support [16]. However, the authors noted a dearth of high-quality exercise interventions based on the Cochrane Collaboration's Risk of Bias [19] and additional criteria developed by Chambless and Hollon [20]. The review highlighted that the quality of previous evidence was low-to-moderate with a call for replication studies with larger sample sizes since the reviewed studies had an average sample size of approximately 50. The review further called for the use of body-worn accelerometers to complement the measurement of physical activity.

The Fitness, Aging, and STress (FAST) study was primarily designed to measure the effects of a 24-week aerobic exercise intervention on cellular aging mechanisms in familial caregivers [21]. However, the study also offered an opportunity to assess the effects of aerobic exercise on psychological functioning as secondary outcomes. Some of these psychological parameters have been examined in previous research with caregivers, including caregiver burden, depressive symptomatology, social connections (i.e., loneliness and social support), and anger. Here, we investigate whether 24 weeks of aerobic exercise has any effects on these measures in a study with a larger sample size and use of body-worn accelerometers, thus answering the call for replication in higher-quality studies [16]. We also broadened the scope of caregiving questionnaires to include positive aspects of caregiving in addition to caregiver burden, which has been a common focus of previous interventions [22–25]. We also extended our measures to include cognitive-emotional constructs that have been related to depression in the larger psychological literature but, to date, have not been considered in studies with family caregivers or following a physical activity intervention. These cognitive-emotional constructs are primarily considered dispositional in nature but have been shown to be amenable to change through intervention. These constructs include measures of emotion regulation tendencies (i.e., rumination, cognitive reappraisal, and emotion suppression) and expectations-based beliefs about the self and the future (e.g., self-mastery, optimism, and pessimism). This approach allows us to determine which, if any, specific psychological functioning domains may be improved through a high-quality exercise intervention in a vulnerable population.

Higher levels of rumination (i.e., the tendency to perseverate on negative events and thoughts [26]) and emotion suppression (i.e., the suppression of outward expression of emotions [27]) and lower levels of cognitive reappraisal (i.e., changing the evaluation of a situation to alter its emotional impact [27]) have each been linked to measures of poor psychological functioning both concurrently and prospectively [28–34]. In one study of family caregivers of adults with bipolar disorder, rumination accounted for a significant amount of variation between caregiver strain and depression [35]. There is evidence that these emotion regulation strategies can be altered following cognitive behavioral therapies and potentially account for the therapeutic benefits of such therapies in studies with adults with depression [36–38]. In a Phase II randomized controlled trial (RCT), a cognitive behavioral therapy program explicitly supplemented with techniques to address rumination showed significant improvements in residual depression [39]. At present, it remains unclear whether a physical activity program can alter these emotion regulation tendencies.

Similarly, it remains unclear whether physical activity can alter perceptions about personal control (i.e., self-mastery) or beliefs about the future (e.g., optimism and pessimism) that have been associated with depression in previous research [40–42]. Self-mastery is the extent to which a person generally expects that they have

the ability to control life events or situations and attain desirable outcomes as a result [43], and developing a sense of mastery in one's life on a daily basis is a primary goal of cognitive behavioral therapies [44]. Self-mastery is often considered a broader, more general disposition than self-efficacy, which is more clearly defined related to a person's sense that they are able to accomplish a specific behavior or achieve a specific outcome [45, 46]. Optimism and pessimism are the general expectations that the future holds desirable or undesirable outcomes, respectively [47, 48] and evidence suggests that both orientations of expectations can be altered with therapy [49].

Based on previous research, then, the current study sought to add to the current literature on the effects of aerobic exercise on family caregivers' psychological functioning. This was achieved by testing the effects of a 24-week exercise intervention on a suite of measures that have been examined in previous studies, including components of caregiving (i.e., burden and positive aspects of caregiving), well-being measures (i.e., depressive symptomatology and anger), and social connections (i.e., perceived social support and loneliness). We hypothesized, based on the previous literature, that reports of these measures would improve in family caregivers randomized to the aerobic exercise arm of the study compared to those who were randomized to the waitlist control group. Some of the measures included in the current study, however, have yet to be examined in exercise intervention studies with family caregivers and, thus, we took an exploratory approach and refrained from forwarding any hypotheses. By testing emotion regulation (rumination, expressive suppression, and cognitive reappraisal) and expectations-based beliefs (mastery, optimism, and pessimism) as potential outcomes, novel findings may be discovered that could direct future research to reveal potential cognitive-emotional mediators of the health benefits of aerobic exercise for family caregivers.

Methods

Participants

As part of the parent study [21], participants were recruited in the San Francisco Bay Area through several sources, including flyers posted at adult daycare centers and clinics that serve Alzheimer's patients, as well as support groups and events sponsored by the Alzheimer's Association. A total of 290 adults were screened for eligibility. Inclusion criteria consisted of a minimum of 10 hr per week of unpaid care for a family member with Alzheimer's disease or other dementia, and the family member was required to have a life expectancy greater than 1 year. Eligible participants were required to be fluent in English, be between 50 and 75 years of age, have a body mass index (BMI) between 20 and 35 kg/m^2, have weekly access to a computer, and, if female, be postmenopausal. Participants were required to be high stress, which was defined to be at least one-half standard deviation above the national average on the Perceived Stress Scale [50]. Finally, to be eligible, participants could not be meeting the U.S. Department of Health and Human Services guidelines for physical activity of 150 min of moderate or 75 min of vigorous weekly physical activity measured by the Stanford Leisure-Time Activity Categorical Item (L-CAT), a reliable and validated self-report activity scale [51]. Exclusion criteria included medical advice to avoid exercise; the inability to walk a block or climb stairs without feeling dizziness, chest pain, or shortness of breath; positive smoking status at the time of study entry; current use of systemic corticosteroids; cancer diagnosis requiring radiation or chemotherapy in the past 10 years; autoimmune disorders; current cardiovascular disease; current substance dependence or addiction; posttraumatic stress disorder; and an active eating disorder.

Study Design

The primary goal of the FAST study was to examine the effects of an RCT of a 24-week aerobic exercise intervention program on cellular aging mechanisms (i.e., telomerase levels and telomere length) in family caregivers of adults with Alzheimer's disease or another dementia-related condition [21]. Eligibility screening for the FAST study occurred in three phases: (1) telephone assessment of inclusion and exclusion criteria; (2) in-person orientation to review objectives, as well as potential risks and benefits of the study; (3) a one-week stretching run-in trial period to ensure participants had the capacity to move for 15 min during at least four separate days. Following acceptance into the study, participants arrived at the University of California, San Francisco's (UCSF) Clinical and Translational Science Institute for a series of questionnaires and completion of a maximum cardiopulmonary exercise test on a treadmill at increasing speeds until volitional termination. Participants were then randomized into either the aerobic training group or waitlist control group. All baseline measures were repeated 24 weeks later.

Randomization

Participants were randomized at a ratio of 1:1 by employing a permuted block (blocks of four) randomization, placing participants in the exercise group or control group. This study utilized a single blind approach in which the experimenters (e.g., lab personnel) were unaware of group assignment. However, it would have been impossible to blind participants to their assigned group.

Procedures

Exercise intervention

Study-appointed coaches created individualized exercise programs for the participants. These programs began with thrice-weekly 20 min sessions of self-selected activities from a list of recommended activities (e.g., walk, run, hike, bike, and swim) at the lower moderate intensity (individualized at 40% of heart rate reserve). By Week 9, the coaches had gradually increased the exercise volume through the frequency (4–5 per week), intensity (upper moderate zone, 59% of heart rate reserve), and length (minimum 30 min) of the sessions. This program was then maintained for the remaining 15 weeks.

All participants in the aerobic exercise group received a gym membership to any nearby YMCA, an opportunity to receive aerobic fitness videos for home use, an accelerometer (wGT3X-BT Monitor from Actigraph Corporation), and a heart rate monitor. No participant requested copies of the fitness videos for home use. Participants were asked to wear their accelerometers and heart rate monitors at each workout and were provided notebooks to record their workouts as well. At the end of each week, participants uploaded their actigraphy data to the ActiCloud, and their coach emailed them a progress report summarizing their previous week's performance the following morning. Participants were asked to examine any inconsistencies between their actigraphy data and notebooks and report them back. Progress reports were adjusted based on participants' feedback on these inconsistencies. Coaches contacted participants who did not reach their assigned goals for a brief phone call wherein the coach discussed facilitators and barriers to exercising. Participants also received five text messages per week that reminded them to exercise, and the L-CAT questionnaire once per month to assess self-reported changes in exercise behavior.

Waitlist control group

Participants in the control group were asked to not change their exercise patterns during the 24-week intervention. At the end of each month of the study, participants in the control group would complete the L-CAT questionnaire online to measure their current levels of exercise. Following completion of the 24-week study, control participants received free gym memberships and a similar personalized fitness program.

Measures

These scales were completed within 1 week prior to starting the intervention and within 1 week of completion at home using online survey software REDCap.

Components of caregiving

Positive aspects of caregiving. The Positive Aspects of Caregiving Scale was used to measure the various ways that providing care has improved an individuals' life [52]. The 10-item scale uses statements regarding aspects of caregiving (e.g., "caring for [recipient's name] made me feel strong and confident" and "caring for [recipient's name] made me feel more useful"). Respondents rated their level of agreement from 1 ("Disagree a lot") to 5 ("Agree a lot") and a mean score was calculated from all items. The sample scores ranged from 1 to 5 and internal consistency (Cronbach's α) was .92.

Caregiver burden. The burden that participants' felt due to "personal strain" and "role strain" was assessed using the 12-item Zarit Burden Interview [53], allowing for the separation of specific areas of burden (e.g., "do you feel strained when you are around your relative/friend" and "do you feel angry when you are around your relative / friend"). These items were scored based on frequency between 0 ("Never") and 4 ("Nearly always"), then combined as a sum score. While potential scores range from 0 to 48, the present sample ranged from 8 to 45. Internal consistency (Cronbach's α) was .85.

Depressive symptomatology

Participants' depressive symptomatology was assessed using the Patient Health Questionnaire, which has been shown to screen for mild to severe depression [54]. This scale measures the frequency of nine symptoms of depression (e.g., "little interest or pleasure in doing things" and "feeling bad about yourself—or that you are a failure or have let yourself or your family down"). Potential responses ranged from 0 ("Not at all") to 3 ("Nearly every day") using a Likert-type scale. Sum scores were calculated with potential scores ranging from 0 to 27, with cutoffs for major depressive disorder between 8 and 11 [55]. The scores among our sample ranged from 0 to 22. The internal consistency (Cronbach's α) was .81.

Social connections

Loneliness. Loneliness was evaluated using the short-form UCLA Loneliness Scale. This eight-item scale was found to be a valid and reliable replacement of the revised UCLA Loneliness Scale [56]. This questionnaire measures level of frequency to statements regarding isolation and loneliness (e.g., "I often feel unhappy being so withdrawn" and "I often feel that I lack companionship") with responses ranging from 1 ("Never") to 4 ("Always"). Sum scores were produced allowing for potential scores from 8 to 32 (sample range 8–28). The internal consistency (Cronbach's α) was .86.

Perceived social support. A short form of the Social Provisions Scale was used in this study to measure social

support [57]. This 10-item validated scale measures the extent to which an individual thinks they have available support from others. Individuals were asked to rate their level of agreement with statements regarding social support (e.g., "there are people I can depend on to help me if I really need it" and "there is a trustworthy person I could turn to for advice if I were having problems") on a Likert-type scale that ranged from 1 ("Strongly disagree") to 4 ("Strongly agree"). An individual's score was the mean of their responses, with the sample ranging from 1.5 to 4.0. Internal consistency was high (Cronbach's α = .89).

Emotion regulation tendencies

Rumination. The Rumination Scale, developed by Trapnell and Campbell, was used to evaluate participants' levels of rumination and the tendency to focus attention on distressing thoughts, feelings, and experiences [26]. Likert-type scales measured participants' level of agreement to 12 items (e.g., "sometimes it is hard for me to shut off thoughts about myself" and "often I'm playing back over in my mind how I acted in a past situation"). Responses to these items ranged from 1 ("Strongly disagree") to 5 ("Strongly agree"). Mean scores were calculated based on response to the items, with the sample range 1.83–4.08. Internal consistency (Cronbach's α) was high at .93.

Expressive suppression. The Expressive Suppression subscale from the Emotional Regulation Questionnaire [27] was used to measure the tendency to suppress emotional activities (e.g., an outburst or change in facial expression) as a way to regulate the experience of emotion. This subscale contains four items (e.g., "I keep my emotions to myself") scored using the means of a Likert-type scale ranging from 1 ("Strongly disagree") to 7 ("Strongly agree"). The range of the sample was 2.25–6.5. Internal consistency (Cronbach's α) was low at .61.

Cognitive reappraisal. The Cognitive Reappraisal subscale from the Emotional Regulation Questionnaire [27] was used to measure the tendency to reinterpret an emotional stimulus as less negative or shift attention from negative content to more positive ones. This subscale contains six items (e.g., "when I want to feel less negative emotion [such as sadness or anger], I change what I'm thinking about") scored using the means of a Likert-type scale ranging from 1 ("Strongly disagree") to 7 ("Strongly agree"). The range of the sample was 1.5–6.3. Internal consistency (Cronbach's α) was satisfactory at .71.

Trait-like dispositions

Mastery. Mastery was assessed using the Pearlin Mastery Scale [43]. This scale uses seven items to measure the degree to which an individual feels control over their life (e.g., "There is little I can do to change many of the important things in my life," "What happens to me in the future mostly depends on me," and "I have little control over the things that happen to me."). These items were scored on a four-point Likert-Type Scale ranking items between 1 ("Don't agree at all") and 4 ("Agree very much"). Sum scores were created using all items leading to potential scores ranging from 7 to 28 (sample range 10–21). Internal consistency (Cronbach's α) was .78.

Optimism. Participants' levels of optimism were assessed using the Life Orientation Test-Revised [58]. This scale is composed of two separate subscales for each of optimism and pessimism, each with three items and four filler items. Items measuring optimism were positively worded (e.g., "Overall, I expect more good things to happen to me than bad"). Individuals ranked their level of agreement on a five-item scale from 0 ("I agree a lot") to 4 ("I disagree a lot"). Mean scores were calculated from the nonfiller items, and the sample ranged from 1 to 5 and had an internal consistency (Cronbach's α) of .71.

Pessimism. Participants' levels of pessimism were assessed using the Life Orientation Test-Revised [58]. This subscale is composed of three items. Items measuring pessimism were negatively worded (e.g., "If something can go wrong for me, it will") and reverse-coded for analysis. Individuals ranked their level of agreement on a five-item scale from 0 ("I agree a lot") to 4 ("I disagree a lot"). Mean scores were calculated from the three items, and the sample ranged from 1 to 5 and had an internal consistency (Cronbach's α) of .76.

Anger. Trait anger temperament (i.e., an individual's tendency to experience anger without any specific provocation) was measured from a subscale of the State-Trait Anger Expression Inventory [59]. The four items of the subscale (e.g., "I have a fiery temper") were scored on a Likert-type scale of frequency between 1 ("Almost never") and 4 ("Almost always"). A mean score was created based on all items. For the present sample, the range was 1–3. Internal consistency (Cronbach's α) was .78.

Statistical Analysis

All participants who completed the randomization process were included in analyses (i.e., intent-to-treat). Changes in outcome were assessed using linear mixed models as recommended for intervention trials [60] with maximum likelihood estimation; fixed effects for experimental group assignment, time, and the interaction between group and time; and random effects for intercept. The use of these models allows for between-group (i.e., treatment effects) and within-group (i.e., pre–post changes within each arm) comparisons in each analysis. The coding for predictors was time at baseline (0) or the end of study (1) and experimental group, in which participants were either assigned to the control (0) or the aerobic exercise group (1).

Linear mixed models provided four estimated coefficients based on the coding of time and experimental group: first, an estimated intercept (β0) corresponding to the estimated mean value of the outcome when time is 0 (baseline) and experimental group is 0 (control); second, an estimated slope for time (β1) corresponding to the estimated mean difference of Time 1 (end of study) compared to Time 0 (baseline) for Group 0; third, an estimated effect for group (β2) corresponding to the estimated mean difference of Group 1 (aerobic exercise group) compared to Group 0 (control) for Time 0 (baseline); and, finally, an estimated slope for the Time × Group interaction (β3) corresponding to whether the changes over time in the group coded 1 differed significantly from the changes over time in the group coded 0. In other words, β3 identifies whether there is a significant treatment effect. A sensitivity analysis was conducted to compare the treatment-only model (i.e., experimental group assignment, time, and the interaction between group and time) to a treatment and covariate model (i.e., sex, mean-centered age, experimental group assignment, time, and the interaction between group and time). As there were no changes in significance levels, the results of the treatment-only model are reported.

For each model, a marginal effect size (RLMM2) based on the work of Nakagawa and Schielzeth was calculated [61]. This effect size represents a variance explained by only the fixed effects (i.e., time, experimental grouping, and time-by-grouping interaction). In addition to the marginal effect size, the standardized betas and 95% confidence intervals (CIs) of the treatment effect are reported.

The data for depressive symptomatology were winsorized to meet the assumption of normality of residuals in the models. Although there was no change in statistical significance, the depressive symptomatology model showed an improved model fit. Multiple imputation was used to replace the missing values in the data set. This method was chosen due to the relatively low missingness of data. For all analyses, we employed random forest imputation, which replaces missing values based on the aggregate of 500 bootstrapped tree models.

All analyses were performed using R statistical software (Version 3.5.3). Missing values were imputed using the missRanger package [62]. Effect sizes were calculated using the sjstats package [63].

Results

Study Population

Participant recruitment was conducted between March 1, 2014 and December 20, 2015. During this time, a total of 290 caregivers were screened, and 102 were found eligible. A total of 68 participants (55 female) consented, completed our run-in trial period, and were randomized into the study (see Consort Diagram by Puterman et al. [21]). Of the 68 participants, 50% were children of a parent with Alzheimer's or other dementias, 46% were spouses, 3% were siblings, and less than 1% were nieces. Four participants withdrew from the study after randomization, and three did not complete the follow-up questionnaires. The final analysis includes 68 participants at baseline and 61 at follow-up.

Means and standard deviations of each measure at baseline for the waitlist control and experimental groups are shown in Table 1. For baseline and follow-up data, see Supplementary Table 1. Overall, there was a low amount of missingness across all scales. The exceptions to this were caregiver burden (14%) and positive aspects of caregiving (12%), which each had a more notable amount of data missing. Otherwise, all scales were missing less than 5% of observations. Due to the low amount of missingness, data were treated as missing at random. Statistical analyses using Fisher's Exact Test (participants' sex) and *t*-tests (participants' age and reported stress) showed no significant differences between those with data and those missing data for any outcome. See Supplementary Table 2 for percentage of missingness separated by time, experimental group, and outcome.

Outcomes

Caregiving

There was no significant treatment effect for positive aspects of caregiving. However, there was a main effect of time within the aerobic exercise group, which showed a significant increase in reported positive aspects of caregiving over the 6 months of the study. Aerobic exercisers significantly decreased in their reported caregiver burden over the course of the study compared to controls, representing a significant treatment effect. While aerobic exercisers showed a decrease in burden, those in the control group had no significant changes (Table 2). The model for positive aspects of caregiving indicated a very small treatment effect size (RLMM2 = 0.03, standardized beta = 0.16, 95% CI = [−0.01, 0.33]), and the caregiver burden model indicated a small treatment effect (RLMM2 = 0.11, standardized beta = −0.24, 95% CI = [−0.46, −0.02]).

Due to the high proportion of missing data for both caregiver burden and positive aspects of caregiving, multiple imputation may produce biased results. Owing to this, regressions were also run using only those observations with complete data. These casewise deletion sensitivity analyses showed similar treatment effect results for both positive aspects of caregiving (baseline $n = 65$, follow-up $n = 47$, RLMM2 = 0.01, standardized

beta = 0.10, 95% CI = [−0.06, 0.25]) and caregiver burden (baseline n = 63, follow-up n = 45, RLMM2 = 0.10, standardized beta = −0.23, 95% CI = [−0.46, 0.01]).

Depressive symptomatology

Table 2 presents mixed model results indicating significant treatment effects, with aerobic exercisers significantly decreasing their reported depressive symptomatology over the course of the study compared to controls. This model showed a small-sized treatment effect (RLMM2 = 0.13, standardized beta = −0.26, 95% CI = [−0.48, −0.04]). Within-group analyses revealed that only the aerobic exercise group had a significant change in depressive symptomatology.

Social connections

Neither the 24-week change in loneliness nor social support differed significantly between groups. Considering within-group changes, loneliness significantly decreased in both the control and aerobic exercise groups, and social support increased in both groups (Table 2). Models for loneliness (RLMM2 = 0.07, standardized beta = −0.04, 95% CI = [−0.21, 0.14]) and social support (RLMM2 = 0.01, standardized beta = 0.01, 95% CI = [−0.12, 0.14]) were both found to have very small treatment effects.

Emotion regulation tendencies

Whereas the 24-week change in rumination did not differ significantly between groups, there were within-group effects. In both the aerobic exercise group and control group, rumination decreased significantly (Table 2). There were no significant differences between groups in either cognitive reappraisal or expressive suppression, nor were there any significant within-group changes for either construct (Table 2). Models for rumination (RLMM2 = 0.04, standardized beta = −0.04, 95% CI = [−0.19, 0.10]), cognitive reappraisal (RLMM2 < 0.01, standardized beta = 0.04, 95% CI = [−0.15, 0.23]), and expressive suppression (RLMM2 = 0.01, standardized beta = −0.03, 95% CI = [−0.23, 0.16]) were all found to have very small treatment effect sizes.

Trait-like dispositions

There was a significant treatment effect for mastery, in which those in the exercise intervention increased their feelings of mastery, an effect significantly different from those in the control group, who had no change in mastery. There were no significant differences between groups in either optimism or pessimism, nor were there any significant within-group changes in either trait over the course of the study (Table 2). Although there was no treatment effect for trait anger temperament, there was a within-group effect. The aerobic exercise group had significant reduction in reported anger between baseline and after the intervention (Table 2). The model for mastery showed a very small treatment effect size (RLMM2 = 0.04, standardized beta = 0.18, 95% CI = [0.01, 0.35]). Models for optimism (RLMM2 = 0.02, standardized beta = 0.08, 95% CI = [−0.11, 0.28]), pessimism (RLMM2 = 0.02, standardized beta = 0.00, 95% CI = [−0.18, 0.17]), and anger (RLMM2 = 0.01, standardized beta = −0.08, 95% CI = [−0.19, 0.04]) each also indicated very small effects.

Table 1. Baseline measures, after multiple imputation, of participants of the Fitness Aging and Stress (FAST) Study, both pooled and by experimental group

	Overall (n = 68)	Waitlist control group (n = 34)	Aerobic exercise group (n = 34)
Number of females (%)	55 (80.88%)	25 (73.53%)	30 (88.24%)
Age, years (standard deviation [*SD*])	61.29 (6.33)	63.29 (6.39)	59.29 (5.68)
Positive aspects of caregiving, mean (*SD*)	3.47 (0.92)	3.55 (0.96)	3.40 (0.88)
Caregiver burden, total (*SD*)	26.72 (8.07)	24.65 (7.78)	28.79 (7.93)
Depressive symptomatology, total (*SD*)	8.19 (5.06)	7.91 (4.92)	8.47 (5.26)
Depressive symptomatology (winsorized), total (*SD*)	7.80 (4.24)	7.55 (4.13)	8.05 (4.40)
Loneliness, total (*SD*)	19.10 (4.62)	19.18 (4.40)	19.03 (4.90)
Social support, mean (*SD*)	3.17 (0.58)	3.17 (0.67)	3.17 (0.49)
Rumination, mean (*SD*)	3.18 (0.63)	3.12 (0.61)	3.23 (0.64)
Expressive suppression, mean (*SD*)	4.42 (0.90)	4.44 (0.94)	4.40 (0.87)
Cognitive reappraisal, mean (*SD*)	3.86 (0.83)	3.90 (0.86)	3.82 (0.82)
Mastery, total (*SD*)	20.42 (4.35)	20.59 (4.24)	19.88 (4.50)
Pessimism, mean (*SD*)	1.39 (0.97)	1.26 (0.95)	1.51 (0.99)
Optimism, mean (*SD*)	2.44 (0.93)	2.41 (1.01)	2.47 (0.86)
Trait anger, mean (*SD*)	1.44 (0.46)	1.41 (0.40)	1.47 (0.52)

Table 2. Treatment effects and between- and within-group changes over 24 weeks in participants randomized to an aerobic exercise experimental group and control arm

Outcome	Unstandardized treatment effect		Change over time in control group		Change over time in aerobic intervention	
	Effect	95% CI	Change	95% CI	Change	95% CI
Positive aspects of caregiving (multiple imputation)	0.34	-0.03, 0.71	0.08	−0.18, 0.31	0.42*	0.15, 0.68
Positive aspects of caregiving (casewise deletion)	0.22	−0.14, 0.59	0.07	−0.20, 0.34	0.27*	0.02, 0.56
Caregiver burden (multiple imputation)	−4.60*	−8.82, −0.38	−1.99	−4.92, 0.95	−6.59*	−9.62, −3.55
Caregiver burden (casewise deletion)	−4.69	−9.58, 0.21	−2.19	−5.52, 1.13	−6.88*	−10.48, −3.29
Depressive symptoms	−2.59*	−4.79, −0.38	−1.43	−2.96, 0.10	−4.02*	−5.60, −2.43
Loneliness	−0.43	−2.40, 1.54	−2.25*	−3.61, −0.89	−2.68*	−4.10, −1.26
Social support	0.02	−0.16, 0.19	0.13*	0.01, 0.25	0.14*	0.02, 0.27
Rumination	−0.06	−0.27, 0.15	−0.19*	−0.33, −0.04	−0.25*	−0.40, −0.10
Emotional regulation						
Expressive suppression	−0.07	−0.52, 0.38	0.19	−0.13, 0.50	0.11	−0.21, 0.44
Cognitive reappraisal	0.08	−0.31, 0.47	−0.04	−0.31, 0.23	0.05	−0.23, 0.33
Mastery	1.78*	0.09, 3.46	0.48	−0.69, 1.65	2.26*	1.04, 3.48
Optimism	0.19	−0.24, 0.61	0.09	−0.20, 0.39	0.28	−0.02, 0.59
Pessimism	−0.01	−0.42, 0.41	−0.04	−0.33, 0.25	−0.05	−0.35, 0.25
Anger	−0.08	−0.20, 0.04	−0.04	−0.13, 0.04	−0.12*	−0.21, −0.03

CI confidence interval.

*$p < .05$.

Discussion

This study sought to better understand the changes in psychological functioning that may occur in response to aerobic exercise in a highly stressed sample of caregivers of older adults. Previous analyses with this sample demonstrated that 24 weeks of aerobic exercise increased participants' physical activity to meet the recommended guidelines on average and significant treatment effects in the exercise group of participants compared to those in the control group on the secondary outcomes of telomere length, cardiopulmonary fitness, BMI, and perceived chronic stress but no significant treatment effects on the primary outcome of telomerase activity levels [21]. The current report demonstrated treatment effects for improving caregiver burden, depressive symptomatology, and mastery. Additionally, those in the exercise group significantly reduced feelings of loneliness, rumination, and anger while increasing their feelings of social support and positive feelings regarding caregiving. Overall, there were no changes in expressive suppression, cognitive reappraisal, optimism, or pessimism.

Our investigation expands on the current literature by assessing multiple aspects of psychological functioning in family caregivers who complete 24 weeks of an aerobic exercise program. In a descriptive review by Lambert et al. [16], there was inconclusive evidence as to whether exercise interventions result in decreased subjective distress and burden and increases in psychological functioning. Lambert et al. noted the lack of high-quality studies in their systematic review. The present study provides additional data in support of an exercise program improving respondent's feelings of caregiver burden, depressive symptomatology, and mastery.

Caregiving has been shown to have measurable negative effects on emotional health, physical health, social life, and financial status [64]. For caregivers, this burden has been associated with depression [65] and mortality [6, 66]. Additionally, previous research found that care recipients with highly burdened caregivers also had a greater risk of mortality [67]. In previous randomized control trials, the effects of exercise interventions on burden have been mixed. Some studies have found that exercise had a significant effect of burden reduction [68–71], while others have noted a lack of effect [17, 18, 24, 72, 73]. This discrepancy is perhaps due to the dose of exercise prescribed either in terms of intensity or duration. Previous research in the general population has shown that exercise has a dose-response relationship with psychological distress such that the greatest reductions in risk of psychological distress occurred at high volumes and/or intensities of exercise [74]. Previous studies that did not find a reduction in burden among caregivers either prescribed low-to-moderate intensity exercise [18, 72] or had a sample that was already meeting physical activity guidelines [73]. Two other studies prescribed 120–160 min of vigorous exercise [17, 24]. However, the interventions mostly employed brisk walking, which is

commonly classified in the lower end of moderate exercise and, thus, was likely not as vigorous as intended. In contrast, in one study that prescribed 180 min of low-to-moderate intensity exercise, there was a decrease in reported burden [69]. The present trial instructed participants to exercise for 150 min per week at the upper end of moderate intensity, which was a higher dose (e.g., longer duration of intervention, higher intensity of exercise, or more exercise per week) than all but two previous RCTs [24, 73]. Furthermore, unlike previous studies that used self-reported physical activity, the dose of exercise in the FAST study, in which these data were collected, was validated using accelerometry and daily reports recorded by the participants, providing more objective and reliable reporting of workouts completed.

The extant literature has found that exercise has no effect on depressive symptomatology in family caregivers [17, 18, 24, 68, 70, 75]. To the best of our knowledge, only one RCT found a treatment effect of exercise on depression [76]. The difference between our study and prior studies is likely partially due to the differences in methodology described above. However, it is also possible that our study found significant differences that were not seen in the majority of previous studies due to our specific sample. We recruited only highly stressed individuals; as stress is positively associated with depression [77], our sample may have had greater baseline depressive symptomatology than other studies. Thus, other studies may have demonstrated a floor effect, in which smaller nonsignificant reductions were seen because baseline levels were lower. Our study did not collect depression diagnosis data from our participants and interested adults who were ineligible for lower stress levels and, thus, we cannot investigate this possibility.

It is also possible that the reported effects on caregiver burden and depressive symptomatology were partially driven by the changes in mastery or general sense of personal control. Previous research has shown that mastery is negatively associated with burden [78] and depression [79] in caregivers. However, the potential effects on mastery have been understudied in the analyses of physical activity interventions in the caregiver population. This is highlighted by the studies reviewed by Lambert et al. [16], in which no studies measured mastery or motivation and only two measured exercise-specific self-efficacy. Future research should assess these relationships for potential mediation effects.

The current study has several strengths. First, as reported in our previous work [21], participants had a high level of adherence to the exercise program as measured by accelerometers worn each time participants exercised (81% at ≥120 min of moderate to vigorous per week; 73% at ≥150 min of moderate to vigorous per week). The majority of previous studies used self-report or pedometers to test adherence to exercise protocols. Exercise adherence using self-reports should be interpreted with caution as a recent systematic review has shown self-reports to have variable levels of criterion validity for exercise behaviors [80]. Furthermore, pedometers have been shown to be less accurate than accelerometers in populations that walk with a slower gait, such as older adults [81]. Our participants were, on average, 61 years old, and 34% were 65 or older. Second, this study used multilevel modeling, which is a robust analysis that allows for the reporting of treatment effects and improves upon previous work that used paired sample tests that cannot report true treatment effects [70, 82]. By reporting interaction (i.e., treatment) effects, the results of the present study can be better incorporated into future meta-analytic works.

This study is not without limitations. We were unable to identify the underlying psychological or biological mechanisms that promote the apparent benefit to psychological functioning. While it is likely that exercise is primarily responsible due to brain-altering effects [83], it is also possible that the lifestyle structure and support provided by the intervention coaches [75, 84] could underlie some of the measured improvements in psychological functioning. Second, as this is not a primary analysis of the parent study, the study was not powered for these analyses. It is conceivable that, with a larger sample, one or more of the within-group effects seen only in the intervention arm (i.e., anger and positive aspects of caregiving) might represent significant treatment effects. Third, we are unable to explain the lack of effects on emotional regulation, optimism, and pessimism. It is possible that there is truly no effect of exercise on dispositional constructs in highly stressed caregivers. However, it is also possible that these effects take longer than 6 months to become apparent given the more dispositional nature of these factors. Fourth, a large proportion of the data for caregiver burden and positive aspects of caregiving was missing. We have presented the results from both the imputed and nonimputed data sets and the results were consistent across procedures. Finally, a large proportion of the study sample was female and, thus, perhaps these results are not representative of all caregivers. While the percentage of male caregivers providing care to an older adult with dementia has decreased in the past two decades from 27.6% to 21.4% [85], future studies should seek to actively recruit equal proportions of men to women to determine the extent to which physical activity impacts both genders.

Conclusion

A 24-week exercise intervention can be an effective treatment for decreasing caregiver burden and depressive symptomatology and increasing mastery in high-stress

caregivers. More research is required to assess whether there may be additional benefits, such as decreased rumination and anger and increased feelings of positive aspects of caregiving. Given the global burden of caregiving, discovering nonpharmaceutical methods for ameliorating caregiver psychological functioning is essential, and aerobic exercise is proving to be one such approach.

Supplementary Material

Supplementary material is available at *Annals of Behavioral Medicine* online.

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Compliance With Ethical Standards

Authors' Statement of Conflict of Interest and Adherence to Ethical Standards The authors declare that they have no conflict of interest.

Authors' Contributions B.A.H. completed data analyses and wrote the first draft. E.J.B. edited the drafts. J.W. and S.S. managed participant engagement and data collection. K.L.J. was the study physician and edited drafts. E.S.E. supported design of the study and edited drafts. E.P. was the principal investigator of the study.

Ethical Approval The study was approved by UCSF's Human Research Protection Program Committee on Human Research (IRB# 13-11322) as well as the UBC Clinical Research Ethics Board (CREB # H16-01094) and was preregistered on clinicaltrials.gov (#NCT01993082).

Informed Consent All study participants gave informed consent prior to beginning the study.

References

1. Ortman JM, Velkoff VA, Hogan H. *An aging nation: the older population in the United States*. Suitland, MD: United States Census Bureau, Economics and Statistics Administration, US Department of Commerce; 2014.
2. Niccoli T, Partridge L. Ageing as a risk factor for disease. *Curr Biol.* 2012;22:R741–R752.
3. Chari AV, Engberg J, Ray KN, Mehrotra A. The opportunity costs of informal elder-care in the United States: New estimates from the American Time Use Survey. *Health Serv Res.* 2015;50:871–882.
4. AARP. Caregiving in the US. Available at https://www.aarp.org/content/dam/aarp/ppi/2015/caregiving-in-the-united-states-2015-report-revised.pdf. Published June, 2015. Accessibility verified June 27, 2017.
5. Lee S, Colditz GA, Berkman LF, Kawachi I. Caregiving and risk of coronary heart disease in U.S. women: A prospective study. *Am J Prev Med.* 2003;24:113–119.
6. Schulz R, Beach SR. Caregiving as a risk factor for mortality: The Caregiver Health Effects Study. *JAMA.* 1999;282:2215–2219.
7. Richardson TJ, Lee SJ, Berg-Weger M, Grossberg GT. Caregiver health: Health of caregivers of Alzheimer's and other dementia patients. *Curr Psychiatry Rep.* 2013;15:367.
8. Schulz R, Martire LM. Family caregiving of persons with dementia: Prevalence, health effects, and support strategies. *Am J Geriatr Psychiatry.* 2004;12:240–249.
9. Pinquart M, Sörensen S. Differences between caregivers and noncaregivers in psychological health and physical health: A meta-analysis. *Psychol Aging.* 2003;18:250–267.
10. Mausbach BT, Chattillion EA, Roepke SK, Patterson TL, Grant I. A comparison of psychosocial outcomes in elderly Alzheimer caregivers and noncaregivers. *Am J Geriatr Psychiatry.* 2013;21:5–13.
11. Sörensen S, Pinquart M, Duberstein P. How effective are interventions with caregivers? An updated meta-analysis. *Gerontologist.* 2002;42:356–372.
12. Adelman RD, Tmanova LL, Delgado D, Dion S, Lachs MS. Caregiver burden: A clinical review. *JAMA.* 2014;311:1052–1060.
13. Sofi F, Valecchi D, Bacci D, et al. Physical activity and risk of cognitive decline: A meta-analysis of prospective studies. *J Intern Med.* 2011;269:107–117.
14. Mammen G, Faulkner G. Physical activity and the prevention of depression: A systematic review of prospective studies. *Am J Prev Med.* 2013;45:649–657.
15. Arem H, Moore SC, Patel A, et al. Leisure time physical activity and mortality: A detailed pooled analysis of the dose-response relationship. *JAMA Intern Med.* 2015;175:959–967.
16. Lambert SD, Duncan LR, Kapellas S, et al. A descriptive systematic review of physical activity interventions for caregivers: Effects on caregivers' and care recipients' psychosocial outcomes, physical activity levels, and physical health. *Ann Behav Med.* 2016;50:907–919.
17. King AC, Brassington G. Enhancing physical and psychological functioning in older family caregivers: The role of regular physical activity. *Ann Behav Med.* 1997;19:91–100.
18. Connell CM, Janevic MR. Effects of a telephone-based exercise intervention for dementia caregivers wives. *J Appl Gerontol.* 2009;28:171–194.
19. Higgins JPT, Green S, eds. *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]*. The Cochrane Collaboration; 2011. Available from www.handbook.cochrane.org.
20. Chambless DL, Hollon SD. Defining empirically supported therapies. *J Consult Clin Psychol.* 1998;66:7–18.
21. Puterman E, Weiss J, Lin J, et al. Aerobic exercise lengthens telomeres and reduces stress in family caregivers: A randomized controlled trial—Curt Richter Award Paper 2018. *Psychoneuroendocrinology.* 2018;98:245–252.
22. King AC, Baumann K, O'Sullivan P, Wilcox S, Castro C. Effects of moderate-intensity exercise on physiological, behavioral, and emotional responses to family caregiving: A randomized controlled trial. *J Gerontol A Biol Sci Med Sci.* 2002;57:M26–M36.
23. Hirano A, Suzuki Y, Kuzuya M, et al. Association between the caregiver's burden and physical activity in community-dwelling

caregivers of dementia patients. *Arch Gerontol Geriatr.* 2011;52:295–298.
24. Castro CM, Wilcox S, O'Sullivan P, Baumann K, King AC. An exercise program for women who are caring for relatives with dementia. *Psychosom Med.* 2002;64:458–468.
25. Hill K, Smith R, Fearn M, Rydberg M, Oliphant R. Physical and psychological outcomes of a supported physical activity program for older carers. *J Aging Phys Act.* 2007;15:257–271.
26. Trapnell PD, Campbell JD. Private self-consciousness and the five-factor model of personality: Distinguishing rumination from reflection. *J Pers Soc Psychol.* 1999;76:284–304.
27. Gross JJ, John OP. Individual differences in two emotion regulation processes: Implications for affect, relationships, and well-being. *J Pers Soc Psychol.* 2003;85:348–362.
28. McLaughlin KA, Nolen-Hoeksema S. Rumination as a transdiagnostic factor in depression and anxiety. *Behav Res Ther.* 2011;49:186–193.
29. Nolen-Hoeksema S, McBride A, Larson J. Rumination and psychological distress among bereaved partners. *J Pers Soc Psychol.* 1997;72:855–862.
30. Aldao A, Nolen-Hoeksema S, Schweizer S. Emotion-regulation strategies across psychopathology: A meta-analytic review. *Clin Psychol Rev.* 2010;30:217–237.
31. Troy AS, Wilhelm FH, Shallcross AJ, Mauss IB. Seeing the silver lining: Cognitive reappraisal ability moderates the relationship between stress and depressive symptoms. *Emotion.* 2010;10:783–795.
32. John OP, Gross JJ. Healthy and unhealthy emotion regulation: Personality processes, individual differences, and life span development. *J Pers.* 2004;72:1301–1333.
33. Moore SA, Zoellner LA, Mollenholt N. Are expressive suppression and cognitive reappraisal associated with stress-related symptoms? *Behav Res Ther.* 2008;46:993–1000.
34. Dryman MT, Heimberg RG. Emotion regulation in social anxiety and depression: A systematic review of expressive suppression and cognitive reappraisal. *Clin Psychol Rev.* 2018;65:17–42.
35. Perlick DA, Gonzalez J, Michael L, et al. Rumination, gender, and depressive symptoms associated with caregiving strain in bipolar disorder. *Acta Psychiatr Scand.* 2012;126:356–362.
36. Southwick SM, Charney DS. The science of resilience: Implications for the prevention and treatment of depression. *Science.* 2012;338:79–82.
37. Troy AS, Shallcross AJ, Davis TS, Mauss IB. History of mindfulness-based cognitive therapy is associated with increased cognitive reappraisal ability. *Mindfulness (N Y).* 2013;4:213–222.
38. Clark DA, Beck AT. Cognitive theory and therapy of anxiety and depression: Convergence with neurobiological findings. *Trends Cogn Sci.* 2010;14:418–424.
39. Watkins ER, Mullan E, Wingrove J, et al. Rumination-focused cognitive-behavioural therapy for residual depression: Phase II randomised controlled trial. *Br J Psychiatry.* 2011;199:317–322.
40. Vickers KS, Vogeltanz ND. Dispositional optimism as a predictor of depressive symptoms over time. *Pers Individ Dif.* 2000;28:259–272.
41. Marshall GN, Lang EL. Optimism, self-mastery, and symptoms of depression in women professionals. *J Pers Soc Psychol.* 1990;59:132–139.
42. Chang EC, Sanna LJ. Optimism, pessimism, and positive and negative affectivity in middle-aged adults: A test of a cognitive-affective model of psychological adjustment. *Psychol Aging.* 2001;16:524–531.
43. Pearlin LI, Schooler C. The structure of coping. *J Health Soc Behav.* 1978;19:2–21.
44. Rector NA. *Cognitive-Behavioural Therapy: An Information Guide*. Toronto, Ontario: Centre for Addiction and Mental Health; 2010.
45. Bandura A. Self-efficacy: Toward a unifying theory of behavioral change. *Psychol Rev.* 1977;84:191–215.
46. Bandura A. Social cognitive theory: An agentic perspective. *Annu Rev Psychol.* 2001;52:1–26.
47. Scheier ME, Carver CS. Dispositional optimism and physical well-being: The influence of generalized outcome expectancies on health. *J Pers.* 1987;55:169–210.
48. Marshall GN, Wortman CB, Kusulas JW, Hervig LK, Vickers RR. Distinguishing optimism from pessimism: Relations to fundamental dimensions of mood and personality. *J Pers Soc Psychol.* 1992;62:1067–1074
49. Carver CS, Scheier MF, Segerstrom SC. Optimism. *Clin Psychol Rev.* 2010;30:879–889.
50. Cohen S, Janicki-Deverts D. Who's stressed? Distributions of psychological stress in the United States in probability samples from 1983, 2006, and 2009. *J Appl Soc Psychol.* 2012;42:1320–1334.
51. Kiernan M, Schoffman DE, Lee K, et al. The Stanford leisure-time activity categorical item (L-Cat): A single categorical item sensitive to physical activity changes in overweight/obese women. *Int J Obes (Lond).* 2013;37:1597–1602.
52. Tarlow BJ, Wisniewski SR, Belle SH, Rubert M, Ory MG, Gallagher-Thompson D. Positive aspects of caregiving: Contributions of the REACH project to the development of new measures for Alzheimer's caregiving. *Res Aging.* 2004;26:429–453.
53. Branger C, O'Connell ME, Morgan DG. Factor analysis of the 12-Item Zarit Burden Interview in caregivers of persons diagnosed with dementia. *J Appl Gerontol.* 2016;35:489–507.
54. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: Validity of a brief depression severity measure. *J Gen Intern Med.* 2001;16:606–613.
55. Manea L, Gilbody S, McMillan D. Optimal cut-off score for diagnosing depression with the Patient Health Questionnaire (PHQ-9): A meta-analysis. *CMAJ.* 2012;184:E191–E196.
56. Hays RD, DiMatteo MR. A short-form measure of loneliness. *J Pers Assess.* 1987;51:69–81.
57. Caron J. [A validation of the Social Provisions Scale: The SPS-10 items]. *Sante Ment Que.* 2013;38:297–318.
58. Scheier MF, Carver CS, Bridges MW. Distinguishing optimism from neuroticism (and trait anxiety, self-mastery, and self-esteem): A reevaluation of the Life Orientation Test. *J Pers Soc Psychol.* 1994;67:1063–1078.
59. Forgays DK, Spielberger CD, Ottaway SA, Forgays DG. Factor structure of the State-Trait Anger Expression Inventory for middle-aged men and women. *Assessment.* 1998;5:141–155.
60. Chakraborty H, Gu H. *A Mixed Model Approach for Intent-to-Treat Analysis in Longitudinal Clinical Trials With Missing Values*. Research Triangle Park: RTI Press; 2009 doi:10.3768/rtipress.2009.mr.0009.0903.
61. Nakagawa S, Schielzeth H. A general and simple method for obtaining R2 from generalized linear mixed-effects models. *Methods Ecol Evol.* 2013;4:133–142.
62. Mayer M. *missRanger: Fast Imputation of Missing Values. R package version 1.0.3.* https://CRAN.R-project.org/package=missRanger. Published May 15, 2018. Accessed September 13, 2018
63. Ludecke D. *sjstats: Collection of Convenient Functions for Common Statistical Computations. R package version 0.17.4.*

https://CRAN.R-project.org/package=sjstats. Published March 15, 2019. Accessed April 23, 2019
64. Zarit SH, Todd PA, Zarit JM. Subjective burden of husbands and wives as caregivers: A longitudinal study. *Gerontologist.* 1986;26:260–266.
65. Souza ALR, Guimarães RA, de Araújo Vilela D, et al. Factors associated with the burden of family caregivers of patients with mental disorders: A cross-sectional study. *BMC Psychiatry.* 2017;17:353.
66. Perkins M, Howard VJ, Wadley VG, et al. Caregiving strain and all-cause mortality: Evidence from the REGARDS study. *J Gerontol B Psychol Sci Soc Sci.* 2013;68:504–512.
67. Kuzuya M, Enoki H, Hasegawa J, et al. Impact of caregiver burden on adverse health outcomes in community-dwelling dependent older care recipients. *Am J Geriatr Psychiatry.* 2011;19:382–391.
68. Hirano A, Suzuki Y, Kuzuya M, Onishi J, Ban N, Umegaki H. Influence of regular exercise on subjective sense of burden and physical symptoms in community-dwelling caregivers of dementia patients: A randomized controlled trial. *Arch Gerontol Geriatr.* 2011;53:e158–e163.
69. Canonici AP, Andrade LP, Gobbi S, Santos-Galduroz RF, Gobbi LT, Stella F. Functional dependence and caregiver burden in Alzheimer's disease: A controlled trial on the benefits of motor intervention. *Psychogeriatrics.* 2012;12:186–192.
70. Varambally S, Vidyendaran S, Sajjanar M, et al. Yoga-based intervention for caregivers of outpatients with psychosis: A randomized controlled pilot study. *Asian J Psychiatr.* 2013;6:141–145.
71. Lowery D, Cerga-Pashoja A, Iliffe S, et al. The effect of exercise on behavioural and psychological symptoms of dementia: The EVIDEM-E randomised controlled clinical trial. *Int J Geriatr Psychiatry.* 2014;29:819–827.
72. Marsden D, Quinn R, Pond N, et al. A multidisciplinary group programme in rural settings for community-dwelling chronic stroke survivors and their carers: A pilot randomized controlled trial. *Clin Rehabil.* 2010;24:328–341.
73. Farran CJ, Paun O, Cothran F, et al. Impact of an individualized physical activity intervention on improving mental health outcomes in family caregivers of persons with dementia: A randomized controlled trial. *AIMS Med Sci.* 2016;3:15–31.
74. Hamer M, Stamatakis E, Steptoe A. Dose-response relationship between physical activity and mental health: The Scottish Health Survey. *Br J Sports Med.* 2009;43:1111–1114.
75. Cuthbert CA, King-Shier KM, Ruether JD, et al. The effects of exercise on physical and psychological outcomes in cancer caregivers: Results from the RECHARGE randomized controlled trial. *Ann Behav Med.* 2018;52:645–661.
76. Danucalov MAD, et al. A yoga and compassion meditation program reduces stress in familial caregivers of Alzheimer's disease patients. *Evid Based Complement Alternat Med.* 2013.
77. Hammen C. Stress and depression. *Annu Rev Clin Psychol.* 2005;1:293–319.
78. Chan EY, Glass G, Chua KC, Ali N, Lim WS. Relationship between mastery and caregiving competence in protecting against burden, anxiety and depression among caregivers of frail older adults. *J Nutr Health Aging.* 2018;22:1238–1245.
79. Schreiner AS, Morimoto T. The relationship between mastery and depression among Japanese family caregivers. *Int J Aging Hum Dev.* 2003;56:307–321.
80. Silsbury Z, Goldsmith R, Rushton A. Systematic review of the measurement properties of self-report physical activity questionnaires in healthy adult populations. *BMJ Open.* 2015;5:e008430.
81. Le Masurier GC, Tudor-Locke C. Comparison of pedometer and accelerometer accuracy under controlled conditions. *Med Sci Sports Exerc.* 2003;35:867–871.
82. Hirano A, Umegaki H, Suzuki Y, Hayashi T, Kuzuya M. Effects of leisure activities at home on perceived care burden and the endocrine system of caregivers of dementia patients: A randomized controlled study. *Int Psychogeriatr.* 2016;28:261–268.
83. Rethorst CD, Wipfli BM, Landers DM. The antidepressive effects of exercise a meta-analysis of randomized trials. *Sport. Med.* 2009;39:491–511.
84. Badger T, Segrin C, Dorros SM, Meek P, Lopez AM. Depression and anxiety in women with breast cancer and their partners. *Nurs Res.* 2007;56:44–53.
85. Wolff JL, Mulcahy J, Huang J, Roth DL, Covinsky K, Kasper JD. Family Caregivers of Older Adults, 1999-2015: Trends in characteristics, circumstances, and role-related appraisal. *Gerontologist.* 2018;58:1021–1032.