Self-Administered Acupressure for Caregivers of Older Family Members: A Randomized Controlled Trial

Running title: Acupressure for Caregiver Stress

Denise Shuk Ting Cheung[1], PhD; Agnes Tiwari[2], PhD; Wing-Fai Yeung[3], PhD; Doris Sau Fung Yu[4], PhD; Mike Ka Pui So[5], PhD; Pui Hing Chau[1], PhD; Xiao-Min Wang[6], PhD; Terry Yat Sang Lum[7], PhD; Helina Yin King Yuk Fung[8], MSoSc; Benson Yuk Ming Ng[8], MSoSc; Zhang-Jin Zhang[9], PhD; Lixing Lao*[9], PhD

[1] School of Nursing, Li Ka Shing Faculty of Medicine, The University of Hong Kong, 21 Sassoon Road, Hong Kong, China

[2] School of Nursing, Hong Kong Sanatorium & Hospital, 11/F, One Island South, 2 Heung Yip Road, Wong Chuk Hang, Hong Kong, China

[3] School of Nursing, The Hong Kong Polytechnic University, Hung Hom, Kowloon, Hong Kong, China

[4] The Nethersole School of Nursing, The Chinese University of Hong Kong, 6/F, Esther Lee Building, The Chinese University of Hong Kong, Shatin, New Territories, Hong Kong, China

[5] Department of Information Systems, Business Statistics and Operations Management, Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong, China

[6] Department of Anaesthesiology, Li Ka Shing Faculty of Medicine, The University of Hong Kong, 102 Pokfulam Road, Hong Kong, China

[7] Department of Social Work and Social Administration, The University of Hong Kong, Jockey Club Tower, The Centennial Campus, Pokfulam, Hong Kong, China

[8] Hong Kong Sheng Kung Hui Lady MacLehose Centre, No. 22, Wo Yi Hop Road, Kwai Chung, New Territories, Hong Kong, China

[9] School of Chinese Medicine, Li Ka Shing Faculty of Medicine, The University of Hong Kong, 10 Sassoon Road, Pokfulam, Hong Kong, China

* Corresponding author:

Professor Lixing Lao

School of Medicine, University of Maryland, 520 W. Lombard Street, East Hall, Baltimore, MD 21201

School of Chinese Medicine, The University of Hong Kong, 21 Sassoon Road, Hong Kong, China

Email: llao@compmed.umm.edu; Tel.: (410) 706-6187

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ABSTRACT

Objective: To test whether self-administered acupressure reduces stress and stress-related symptoms in caregivers of older family members.

Design: In this randomized, assessor-blind, controlled trial, 207 participants were randomized (1:1) to an acupressure intervention or a waitlist control group.

Setting: Community centers in Hong Kong.

Participants: Primary caregivers of an older family member who screened positive for caregiver stress with symptoms of fatigue, insomnia, or depression.

Intervention: The 8-week intervention comprised four training sessions on self-administered acupressure, two follow-up sessions for learning reinforcement, and daily self-practice of self-administered acupressure.

Measurements: The primary outcome was caregiver stress (Caregiver Burden Inventory). Secondary outcomes included fatigue (Piper Fatigue Scale), insomnia (Pittsburgh Sleep Quality Index), depression (Patient Health Questionnaire), and health-related quality of life (12-item Short-Form Health Survey version 2). An intention-to-treat analysis was adopted.

Results: Of 207 participants, 201 completed the study. Caregiver stress in the intervention group was significantly lower than that in the control group after 8 weeks (difference = -8.12; 95% CI, -13.20 to -3.04; $P = 0.002$) and at 12-week follow-up (difference = -8.52; 95% CI, -13.91 to -3.12; $P = 0.002$). The intervention group, relative to the control group, also had significantly improved secondary outcomes of fatigue (difference = -0.84; 95% CI, -1.59 to -0.08; $P = 0.031$), insomnia (difference = -1.34; 95% CI, -2.40 to -0.27; $P = 0.014$), depression (difference = -1.76; 95% CI, -3.30 to -0.23; $P = 0.025$), and physical health-related quality of life (difference = 3.08; 95% CI, 0.28 to 5.88; $P = 0.032$) after 8 weeks.

Conclusion: Self-administered acupressure intervention significantly relieves self-reported caregiver stress and co-occurring symptoms in those caring for older family members.

Further studies are needed to measure the symptoms objectively and to examine the clinical importance of the observed improvement in caregiver stress.

Trial Registration: ClinicalTrials.gov Identifier NCT02526446.

INTRODUCTION

Population aging is accompanied by an increase in the prevalence of chronic disease and disability among older persons, resulting in a growing demand for care.[1] The primary caregiving role often falls on family members.[2] A substantial body of evidence suggests that family caregivers experience physical and psychological health problems arising from their physically and emotionally demanding caregiving responsibilities.[2-4] Caregiver burden is a multifaceted concept that encompasses the physical, psychological, social, and financial stresses experienced by caregivers due to providing care.[5] Caregiver stress is also commonly used to describe the strain that caregivers face when caring for a person with a chronic disease. However, for some researchers, burden refers to the tangible and concrete aspects of care, and therefore, it is more predominantly used in measurement, while stress relates more to the subjective appraisal of strain on the caregiver.[6] In this paper, caregiver stress conveys the conceptual meaning and caregiver burden is used in measurements, but they refer to the same construct. Caregiver stress is prevalent and often co-occurs with stress-related symptoms such as fatigue, insomnia, and depression.[7] It not only renders family caregivers vulnerable to poor health outcomes, but it is also associated with impaired quality of life (QoL) of caregivers[8] and adverse health outcomes such as higher mortality and hospitalization rates for care recipients.[9] The hazardous impact of caregiver stress necessitates low-risk (i.e., non-pharmacological) measures for managing caregiving-related symptoms.[7]

Acupressure is a non-invasive technique based on the traditional Chinese medicine (TCM) meridian theory.[10] It is defined as the application of pressure using hands or fingers on acupoints located along the meridians (i.e., channels throughout the body which help to

maintain energy [qi] flow). According to TCM theory, through acupressure, meridians are stimulated, leading to opening of the channels and balancing of qi, thus restoring health. From a physiological perspective, research suggests that stimulation of acupuncture points by acupressure increases production of neurotransmitters and hormones such as serotonin and endorphins and it improves cortisol regulation. Such physiological changes activate a parasympathetic nervous system relaxation response and create feelings of calm.[11]

Acupressure can be administered by professional practitioners or by the recipients themselves after undergoing appropriate training. A systematic review has demonstrated the potential effects of self-administered acupressure on relieving symptoms such as stress, fatigue, and insomnia, and it has emphasized the need for well-designed randomized controlled trials (RCTs).[12] Given that caregivers are often limited by time-consuming caregiving tasks, self-administered acupressure, which is a low-cost, safe, flexible, and simple technique, may be used for symptom management. This RCT was conducted to test the effects of a specifically designed self-administered acupressure intervention on alleviating caregiver stress and stress-related symptoms among caregivers of older family members.

METHODS

Trial design, setting, and participants

A previously reported trial protocol [13] was followed. An 8-week randomized controlled trial comparing self-administered acupressure versus a waitlist control was conducted between July 1, 2016 and December 30, 2018. Reporting of this study followed the Consolidated Standards of Reporting Trials guidelines. Participants were recruited from nine community centers that provide diversified health and social services for caregivers in different districts

in Hong Kong. To be eligible for the study, the participants had to be Chinese, aged 21 years or older, able to communicate in Cantonese or Putonghua, acting as the primary caregiver of an older family member aged ≥ 65 years, and providing unpaid care to the care recipient no less than 14 hours per week. In addition, they had to have screened positive for caregiver stress, with symptoms of fatigue, insomnia, or depression based on self-reported questionnaires (Supplemental Table S1).

To confirm a participant's eligibility, a face-to-face or phone interview was conducted by a center-based social worker or a trained research assistant who was not involved in subsequent data collection. All participants provided written informed consent. Ethical approval was obtained from the local ethical committee.

Randomization and blinding

Eligible participants were randomly assigned to either the intervention or the waitlist control group at a 1:1 ratio based on a computerized block randomization process with randomly selected block sizes. The randomization list was recorded and placed in sequentially numbered, sealed, opaque envelopes by an investigator not involved in recruitment. The envelopes were kept by a center staff member not involved in the study as central control to avoid bias in selection. Research assistants conducting data collection and data input were blinded. The data analyst was also blinded.

Intervention and control conditions

The self-administered acupressure protocol used in the present study was based on a systematic review of the literature relating to acupoint selection in symptom management,[14,15] investigators' previous publicationss,[16-18] and consensus meetings of the senior TCM practitioners in the team (WFY, ZJZ, LL). The protocol involves self-

administration of acupressure on nine acupoints (Figure 1). The acupressure procedures have been previously described.[13]

The intervention lasted 8 weeks and comprised of (i) individual training sessions on self-administered acupressure provided by certified trainers, twice a week for 2 weeks; (ii) individual follow-up by certified trainers to reinforce learning and self-practice, weekly for 2 weeks; and (iii) practice of self-administered acupressure by the participant at home, to be undertaken no less than an hour after a meal, for 15 minutes, twice a day for 6 weeks following completion of the 2-week training sessions (Figure 2). Participants were instructed and trained to stimulate the acupoints until they felt soreness, numbness, or heaviness, which are unique sensations interpreted as the flow of qi.[19] However, the force should not be strong enough to produce sharp pain. The trainers, made up of a senior year TCM student and a senior year nursing student, were certified by a licensed TCM practitioner (WFY). During the final training session, the trainers used a competency checklist to assess the participants on their techniques of locating and massaging the acupoints. Given the time restrictions caregivers face, training and follow-up sessions took place in locations (such as the home) and at times preferred by the participants.

To ensure a standardized delivery of intervention, identical training materials, including the acupressure protocol and the poster illustrating the acupoints, were used in each individual training. To monitor compliance, during Weeks 5 through 8 of the intervention, the team of trainers who previously trained the participants made weekly phone calls to remind participants to perform the self-administered acupressure and to answer any questions. Each participant recorded the frequency, duration, and time of the acupressure conducted each day in an acupressure diary and reported the log to the trainer

during the telephone calls. The diary was collected by researchers at the end of the study and double checked against the log recorded by the trainer. Any inconsistency was clarified with the participant.

Participants in the waitlist control group were provided with the option of receiving acupressure training after completion of data collection.

Measures

Data were collected at baseline, post-training (Week 2, i.e., on completion of the 2-week individual training), post-intervention (Week 8, i.e., on completion of the entire self-acupressure intervention), and follow-up (Week 12, i.e., 4 weeks after the completion of the intervention) by administering the following questionnaires to the participants, except the Demographic Questionnaire, which was only administered at baseline.

The primary outcome measure was the validated Chinese version of the Caregiver Burden Inventory (CBI) (24 items).[20] The five components of burden measured were time dependence, developmental burden, physical burden, social burden, and emotional burden, with higher scores indicating higher caregiver stress. A summed score ≥ 25 indicated high caregiver stress.

Secondary outcome measures included fatigue, insomnia, depressive symptoms, and health-related QoL. The validated Chinese version of the Piper Fatigue Scale (PFS) (22 items)[21] was used to assess the levels of fatigue. Scores of 4-6 indicate moderate fatigue, and 7-10 indicate severe fatigue.[22] The Chinese version of the Pittsburgh Sleep Quality Index (PSQI) (19 items)[23] was used to assess severity of insomnia. Higher scores indicate greater degrees of insomnia. A global PSQI score > 5 yielded a diagnostic sensitivity of 89.6% and a specificity of 86.5% in identifying poor sleepers.[24] A reduction of three or more points is

considered the minimal clinically important difference (MCID) for the PSQI.[25] The Chinese version of the Patient Health Questionnaire (PHQ) (9 items)[26] was used to assess levels of depression. Higher scores indicate more severe depressive symptoms. The sensitivity and specificity for a cut-off score of 10 for diagnosing major depressive disorder were 0.85 and 0.89, respectively.[27] The MCID for the PHQ is a reduction of five or more points.[28] The Chinese version of the 12-item Short-Form Health Survey version 2 (SF-12v2) [29] was used to assess health-related QoL. The items are categorized into a mental component summary (MCS) and a physical component summary (PCS). Higher scores indicate a better health status. A mean score of 50 has been articulated as a normative value, meaning that scores > 50 indicate better physical or mental health than the mean, while scores < 50 indicate worse physical or mental health than the mean.[30] The MCID for QoL is an increase in 4.22 or more points on the MCS and PCS of SF-12v2.[31] Three additional items (i.e., use of prescription drugs, incidence of physician visits, and inpatient hospitalization) [32,33] were used to assess participants' healthcare resource use in the past 2 weeks. A demographic questionnaire was used to collect demographic information and caregiving characteristics at baseline.

Sample size

Sample size was calculated based on the primary comparison of caregiver stress scores between the intervention and control groups. With reference to a previous study,[34] we assumed that the mean and standard deviation of the baseline CBI score are 47.54 and 17.61, respectively. A 10-15% reduction in the CBI score, equivalent to a small to medium effect size, was considered a meaningful improvement, thus a difference of six points in the CBI score was anticipated following intervention. Assuming a moderate correlation (P = 0.7) between the pre- and post-measurements of CBI scores, we approximated the pooled

standard deviation of the change in the mean CBI score as $17.61\sqrt{2(1-P)}$ = 13.64. Hence, 83 subjects per group were needed to yield a power greater than 80% and a 5% level of significance. Allowing for an attrition rate of 15%, the target sample size was at least 98 per group. We rounded up the number of participants to 100 per group, and 200 in total.

Statistical analysis

An intention-to-treat (ITT) analysis was adopted. Baseline characteristics between the intervention and the waitlist control groups were assessed by a chi-square test and a *t* test for categorical and continuous data, respectively. The scores of the CBI, PFS, PSQI, PHQ-9, SF-12v2, and HEA were analyzed by a mixed-effects model to examine the differences between the intervention group and the waitlist control group, and changes over time. The interaction between group and time (group × time) was included to examine changes in between-group difference over time. The identity link function was used for continuous variables and the logit link function was used for categorical variables. The mixed-effects model can accommodate missing data without imputation manually, thereby providing a natural way to deal with missing values or dropouts.[35] The Bonferroni adjustment was used for multiple pairwise comparisons. Between-group effect sizes were computed by dividing the difference between group means by the pooled standard deviation. In addition, responder analysis was conducted as follows: (i) For CBI and PFS, due to the absence of an established threshold of clinically meaningful improvement in the literature, the percentage of participants who shifted from high to low caregiver stress and from moderate/severe to mild fatigue was calculated; (ii) For the remaining outcome measures (PHQ, PSQI, and SF12v2), the percentage of participants who achieved clinically meaningful improvement based on MCIDs established in the literature was calculated. A *P* value of less than 0.05 is

considered statistically significant, and all significance tests were two-sided. Statistical analysis was conducted with IBM SPSS version 23.

RESULTS

Participants

Of 1,766 individuals who were assessed for eligibility, 1,559 were excluded for not meeting the inclusion criteria or declined to participate (Figure 2), resulting in a randomized sample of 207 participants (11.7% of those screened). The study was completed by 97.1% (100 of 103) of the participants in the intervention group and 94.1% (101 of 104) of those in the waitlist control group. Overall, six participants (2.9%) withdrew from the study due to lack of time. Of the participants in the intervention group, 83% completed all four training sessions and attended at least one follow-up session. The average daily duration of self-administered acupressure throughout the study was 11.32 (SD 14.92) minutes (equivalent to once daily). The average competency scores of techniques for locating and massaging acupoints were 7.95 (SD 0.38) and 7.86 (SD 0.61) out of 8 marks, respectively. One participant reported low back pain when massaging the UB23 Shenshu (an acupoint located on the back).

At baseline, sociodemographic characteristics (Table 1) and outcome measures (Table 2) between the intervention and waitlist control groups did not differ significantly. All participants' data were analyzed by the original assigned groups.

Primary outcome

Post-intervention CBI scores in the intervention group decreased significantly compared with baseline, by 16.99 points (95% confidence interval [CI], -21.61 to -12.37; $P < 0.001$),

whereas those in the waitlist control group decreased by 10.02 points (95% CI, -14.58 to -5.46; $P < 0.001$) (Table 2). Although there was no significant between-group difference post-training (difference = -4.41; 95% CI, -9.10 to 0.27; $P = 0.07$), the CBI scores of the intervention group were significantly lower than those of the waitlist control group post-intervention (difference = -8.12; 95% CI, -13.20 to -3.04; $P = 0.002$; effect size = -0.44) and follow-up (difference = -8.52; 95% CI, -13.91 to -3.12; $P = 0.002$; effect size = -0.43). There was a significant change in the between-group difference in the CBI scores over time, as indicated by the group × time interaction effect ($P = 0.013$).

Secondary outcomes

Results of analyses of secondary outcomes are presented in Table 3. The PFS, PSQI, and PHQ scores of the intervention group were significantly lower than those of the waitlist control group post intervention (PFS: difference = -0.84; 95% CI, -1.59 to -0.08; $P = 0.031$; PSQI: difference = -1.34; 95% CI, -2.40 to -0.27; $P = 0.014$; PHQ: difference = -1.76; 95% CI, -3.30 to -0.23; $P = 0.025$; Table 3). At follow-up, the between-group differences in PSQI and PHQ scores remained significant (PSQI: difference = -1.28; 95% CI, -2.25 to -0.32; $P = 0.009$; PHQ: difference = -2.40; 95% CI, -3.68 to -1.13; $P < 0.001$). A significant change of between-group difference over time was only observed in the PSQI scores, as indicated by the group × time interaction effect ($P = 0.026$).

Regarding health-related QoL, the between-group difference reflected in the PCS was statistically significant post intervention (difference = 3.08; 95% CI, 0.28 to 5.88; $P = 0.032$) and at follow-up (difference = 3.74; 95% CI, 1.34 to 6.14; $P = 0.002$), while that of the MCS was only statistically significant at follow-up (difference = 4.43; 95% CI, 1.43 to

7.43; $P = 0.004$). Significant change of between-group difference over time was only observed in the PCS, as indicated by the group × time interaction effect ($P = 0.027$).

Regarding healthcare resource use, only inpatient hospitalization showed significant group × time interaction effect ($P < 0.001$), but not for use of prescription drugs and incidence of physician visits (Supplemental Table S2). However, no significant between-group difference was found at all time points. The fitted fixed effects coefficients of the mixed models for healthcare resource use and all outcome measures are shown in Supplemental Tables S2 and S3 respectively.

Responder analysis

The results of the responder analysis are shown in Supplemental Table S4. The proportion of participants shifting from high caregiver stress to low caregiver stress post intervention was significantly higher in the intervention group than that in the control group post intervention (51%% vs. 35.6%; difference = 15.4%; 95% CI, 2% to 28.9%; $P = 0.025$) and at follow-up (51.5% vs. 31.4%; difference = 20.1%; 95% CI, 6.8% to 33.4%; $P = 0.003$).

Among secondary measures, a higher proportion of participants experiencing clinically important improvement post intervention in the intervention group compared to the control group was observed for insomnia (46% vs. 28.4%; difference = 17.6%; 95% CI, 4.4% to 30.7%; $P = 0.009$) and physical health-related QoL (54% vs. 40.2%; difference = 13.85%; 95% CI, 0.1% to 27.5%; $P = 0.048$). At follow-up, more participants in the intervention group showed clinically meaningful improvement post intervention in depression (42.6% vs. 29.4%; difference = 13.2%; 95% CI, 1% to 26.3%; $P = 0.049$) and physical health-related QoL (55% vs. 30.7%; difference = 24.3%; 95% CI, 11% to 37.6%; $P < 0.001$).

DISCUSSION

Our results showed that self-administered acupressure significantly improves caregivers' stress, fatigue, insomnia, depressive symptoms, and physical health-related QoL compared with the waitlist control post intervention. Improvements in the aforementioned outcome measures (except fatigue) were sustained at the 12-week follow-up.

Both the intervention and the control group reported a substantial decrease in caregiver stress at follow-up (-15.74 vs. -8.37 points on the CBI, a 96-point scale). Responder analysis revealed that the proportion of participants who shifted from high to low caregiver stress at follow-up in the acupressure group (51.5%) was significantly greater than that in the control group (31.4%). Compared with the post intervention between-group effect size reported in a recent meta-analysis on the impact of behavioral interventions on reducing caregiver stress vs. an inactive control condition (Hedge's g = -0.18),[36] the effect size of caregiver stress reduction by acupressure (Cohen's d = -0.44) was large. Most of the studies included in the meta-analysis were on education, counselling, cognitive behavioral therapy, and physical activity interventions. Compared to these interventions, our intervention has the advantages of low cost, flexibility, and feasibility. However, further research is needed to understand the clinical importance of the improvement in caregiver stress, as well as the cost-effectiveness of the intervention when adopted in the community.

Preliminary studies examining the effect of acupressure on stress have yielded positive findings in other populations, including patients on hemodialysis,[37] college students,[38] postpartum women,[39] and middle-aged women.[40] However, the mechanisms underlying the positive impact of acupressure remain unexplored. A plausible explanation is that acupressure may modulate the activity of the sympathetic nervous system through the

meridian system.[41] By inhibiting the sympathetic nervous system, stress hormone release decreases, promoting relaxation and stress reduction. However, this mechanism is purely conjectural, and further investigation is required for validation.

The beneficial effect of acupressure on improving fatigue, insomnia, depressive symptoms, and physical health-related QoL as shown in the current study is consistent with that of previous studies.[12,42,43] Of note, responder analysis revealed that significantly more participants in the intervention group reported clinically meaningful improvement in insomnia and physical health-related QoL post intervention, while at follow-up, more intervention group participants showed clinically meaningful benefits in depression and physical health-related QoL than control group participants. The absence of intervention effect on mental scores of QoL post-intervention is possibly attributable to the generic nature of the SF12v2, which may render it less sensitive in measuring the mental health component specific to caregiver stress. While there is evidence to suggest that acupressure affects multiple symptoms in addition to caregiver stress, whether or not these co-occurring symptoms play a mediating role on the intervention effect is unknown and warrants further research.

From a practice perspective, service providers may consider adopting self-administered acupressure as an evidence-based intervention to alleviate caregiver stress and related symptoms. Although there is some uncertainty about the clinical meaning of the observed improvement in caregiver stress, the effect size is comparatively larger than that of other randomized studies of behavioral interventions.[36] The improvements in insomnia and depression are of particular clinical relevance. Importantly, the high retention (97.1%) and adherence reveal that the intervention is acceptable to caregivers. In addition, the successful

training of health-care students to serve as trainers in the study demonstrates the potential for training up service providers to deliver self-administered acupressure training to caregivers. All components of the intervention have been standardized, and training materials have been developed for the service providers. The intervention as a low-cost, safe, flexible, and simple technique may be easily translated into practice with little professional burden.

Despite the robust study design and the low attrition rate, this study has limitations. First, objective measures (e.g., cortisol, actigraphy) were not included because of funding constraints, and future studies should add objective protocols. Second, the extra attention received by participants during training and follow-up of the acupressure practice sessions may have partly contributed to the positive outcomes in the intervention group participants. Third, the study sample only included Chinese caregivers, limiting the generalizability of the findings to other ethnic groups. Fourth, follow-up was limited to 4 weeks post intervention. A longer follow-up period is recommended in future studies. Finally, given that this was not a sham controlled trial, whether the findings are affected by placebo effect is unknown. Future trials should use sham procedures as the control to distinguish more clearly whether intervention is effective beyond the placebo response or other non-specific responses.

The present randomized clinical trial shows statistically significant benefits of self-administered acupressure on relieving self-reported caregiver stress and co-occurring symptoms in those caring for older family members. Further studies are necessary to measure the outcomes objectively, study the mechanisms underlying the improvement, and examine the clinical importance of this effect. Besides, further research is needed to determine the cost-effectiveness and implementability of the acupressure intervention compared to the existing behavioral interventions for caregiver stress reduction.

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Author Contributions:

Study concept and design: Cheung, Tiwari, Yeung, Yu, So, Wang, Lum, Yuk Fung, Zhang, Lao

Acquisition of data: Cheung, Yu, Yuk Fung, Ng

Analysis and interpretation of data: Cheung, So, Chau

Drafting of the manuscript: Cheung, Tiwari, Yeung, Chau, Lao

Critical revision of the manuscript for important intellectual content: Cheung, Tiwari, Yeung, Yu, So, Chau, Wang, Lum, Yuk Fung, Ng, Zhang, Lao

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Figure Legends

Figure 1. Location of acupoints

Figure 2. Study flow

Supplemental Material legends

Supplemental Table S1. Inclusion and exclusion criteria

Supplemental Table S2. Fitted coefficients of fixed effects of the generalized mixed models of items on healthcare resource use

Supplemental Table S3. Fitted coefficients of fixed effects of the mixed models for the primary and secondary outcomes

Supplemental Table S4. Results of responder analysis

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Tables

Table 1. Baseline Characteristics of Participants

	Group, Number (%)		
Background Characteristics of Caregivers	**Intervention (n=103)**	**Control (n=104)**	***P* value**
Age, mean ± SD, years	59.03±11.73	58.97±13.75	.97
Education			.39
≤6 years	23 (22.3%)	30 (28.9%)	
7–13 years	69 (67%)	56 (53.9%)	
Tertiary	11 (10.7%)	18 (17.3%)	
Employed	36 (35%)	37 (35.6%)	.93
Marital status			.58
Single/divorced	35 (34.0%)	37 (35.6%)	
Married/cohabiting	68 (66.0%)	67 (64.4%)	
Number of children, mean ± SD	1.34±1.24	1.53±1.34	.29
Experiencing financial hardship	27(26.2%)	28 (26.9%)	.91
Suffering from chronic illness	38 (36.9%)	47 (45.2%)	.23
Caregiving characteristics	**Intervention (n=103)**	**Control (n=104)**	***P* value**
Total number of care-giving per week (hours), mean ± SD	49.14±49.34	54.25±51.95	.47
Length of caring (months), mean ± SD	77.85±67.17	83.43±62.41	.57
Received assistance from family members for caregiving	58 (56.3%)	63 (60.6%)	.53
Caregiving activities			
Medical assistance	53 (56.4%)	48 (53.3%)	.68
Transport	84 (89.4%)	79 (87.8%)	.74
Food preparation	74 (78.7%)	70 (77.8%)	.88
Self-care activities such as feeding	18 (19.1%)	13 (14.4%)	.39
Personal hygiene such as bathing	32 (34%)	20 (22.2%)	.08
Housekeeping	11 (11.7%)	13 (14.4%)	.58
Home management such as grocery shopping	7 (7.4%)	11 (12.2%)	.28

Table 2. Primary outcome at different time points

	Intervention (n=103)			Control (n=104)			Between-group difference at each time point			Group × time *P* value
	Mean (95% CI)	Within-group change from baseline (95% CI)	*P* value	Mean (95% CI)	Within-group change from baseline (95% CI)	*P* value	Mean (95% CI)	*P* value	Effect size (95% CI)	
CBI[a]										.013
Baseline	41.50 (38.85, 44.14)	/		42.64 (40.01, 45.28)			-1.15 (-4.89, 2.59)	.55		
Post-training	28.77 (25.45, 32.10)	-12.72 (-16.79, -8.67)	<.001	33.18 (29.88, 36.48)	-9.46 (-13.49, -5.44)	<.001	-4.41 (-9.10, 0.27)	.07	-0.26 (-0.53, 0.02)	
Post-intervention	24.51 (20.89, 28.12)	-16.99 (-21.61, -12.37)	<.001	32.63 (29.06, 36.19)	-10.02 (-14.58, -5.46)	<.01	-8.12 (-13.20, -3.04)	.002	-0.44 (-0.71, -0.16)	
Follow-up	25.76 (21.93, 29.59)	-15.74 (-20.44, -11.04)	<.001	34.27 (30.47, 38.07)	-8.37 (-13.04, -3.71)	<.001	-8.52 (-13.91, -3.12)	.002	-0.43 (-0.71, -0.16)	

[a]score range: 0 to 96, higher scores represent higher caregiver stress

Note. CBI: Caregiver Burden Inventory.

Table 3. Secondary outcomes at different time points

	Intervention (n=103)	Control (n=104)	Between-group difference at each time point			Group × time *P* value
	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)	*P* value	Effect size	
PFS[a]						0.45
Baseline	3.16 (2.62, 3.71)	3.56 (3.01, 4.10)	-0.40 (-1.17, 0.37)	.31		
Post-training	1.32 (0.80, 1.84)	2.28 (1.76, 2.80)	-0.96 (-1.69, -0.22)	.011	-0.36	
Post-intervention	1.48 (0.94, 2.02)	2.31 (1.78, 2.84)	-0.84 (-1.59, -0.08)	.031	-0.30	
Follow-up	1.50 (0.97, 2.03)	2.10 (1.57, 2.62)	-0.60 (-1.34, 0.15)	.11	-0.22	
PSQI[b]						.03
Baseline	9.04 (8.31, 9.77)	9.29 (8.56, 10.01)	-0.25 (-1.28, 0.78)	.63		
Post-training	6.79 (6.08, 7.49)	8.46 (7.76, 9.16)	-1.67 (-2.66, -0.68)	.001	-0.45	
Post-intervention	6.91 (6.15, 7.67)	8.25 (7.49, 9.00)	-1.34 (-2.40, -0.27)	.014	-0.35	
Follow-up	5.97 (5.29, 6.66)	7.26 (6.58, 7.93)	-1.28 (-2.25, -0.32)	.009	-0.37	
PHQ[c]						.26
Baseline	8.25 (7.26, 9.24)	9.38 (8.39, 10.36)	-1.12 (-2.52, 0.28)	.12		
Post-training	6.34 (5.29, 7.39)	7.96 (6.92, 9.00)	-1.63 (-3.11, -0.14)	.032	-0.30	
Post-intervention	6.06 (4.97, 7.16)	7.83 (6.75, 8.91)	-1.76 (-3.30, -0.23)	.025	-0.31	
Follow-up	4.78 (3.88, 5.69)	7.19 (6.29, 8.08)	-2.40 (-3.68, -1.13)	<.001	-0.51	
PCS[d]						.027
Baseline	40.36 (38.64, 42.08)	39.96 (38.25, 41.68)	0.40 (-2.03, 2.83)	.75		
Post-training	45.28 (43.45, 47.10)	41.25 (39.44, 43.06)	4.03 (1.46, 6.60)	.002	0.43	
Post-intervention	45.72 (43.73, 47.71)	42.64 (40.66, 44.61)	3.08 (0.28, 5.88)	.032	0.30	
Follow-up	46.30 (44.60, 48.00)	42.56 (40.87, 44.25)	3.74 (1.34, 6.14)	.002	0.19	
MCS[d]						.07
Baseline	41.53 (39.65, 43.40)	40.90 (39.03, 42.77)	0.63 (-2.02, 3.28)	.64		
Post-training	44.65 (42.39, 46.92)	42.77 (40.52, 45.02)	1.88 (-1.31, 5.07)	.25	0.16	
Post-intervention	45.19 (42.93, 47.44)	42.77 (40.53, 45.01)	2.42 (-0.76, 5.59)	.14	0.21	
Follow-up	47.09 (44.16, 49.22)	42.66 (40.54, 44.78)	4.43 (1.43, 7.43)	.004	0.41	

[a] score range: 0 to 10, higher scores represent higher levels of fatigue; [b] score range: 0 to 21, higher scores represent more severe sleep disturbance; ; [c] score range: 0 to 27, higher scores represent more severe depressive symptoms; [d] score range: 0 to 100, higher scores represent higher health-related quality of life

Note. PFS: Piper Fatigue Scale, PSQI: Pittsburgh Sleep Quality Index, PHQ: Patient Health Questionnaire, PCS: physical component summary of 12-item Short-Form Health Survey version 2, MCS: mental component summary of 12-item Short-Form Health Survey version 2

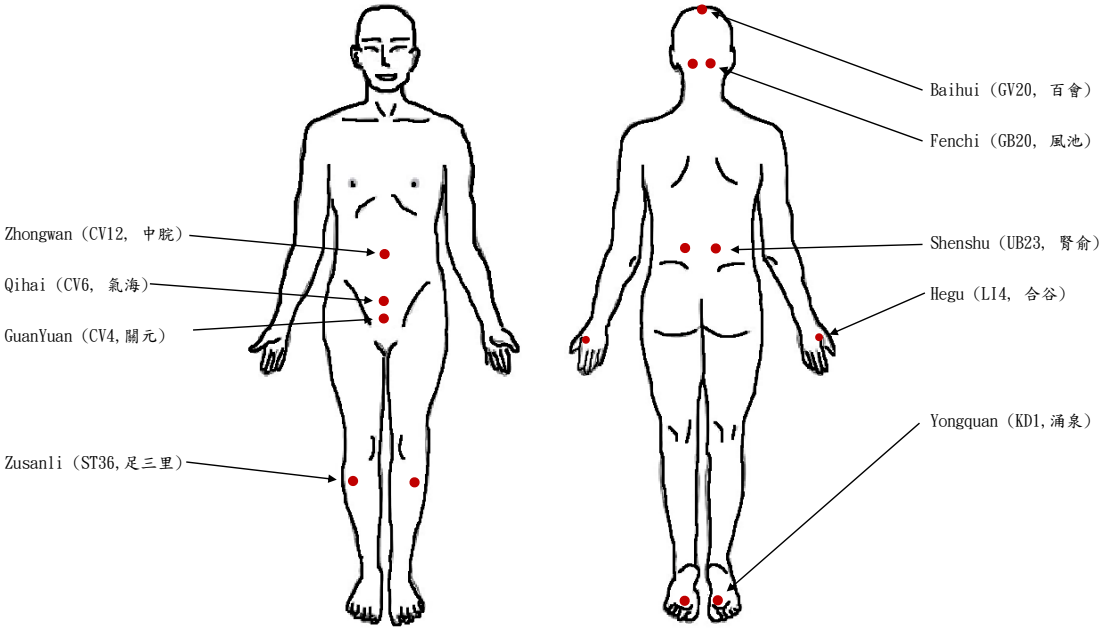
Zhongwan（CV12, 中脘）
Qihai（CV6, 氣海）
GuanYuan（CV4,關元）
Zusanli（ST36,足三里）
Baihui（GV20, 百會）
Fenchi（GB20, 風池）
Shenshu（UB23, 腎俞）
Hegu（LI4, 合谷）
Yongquan（KD1,涌泉）

Figure 1

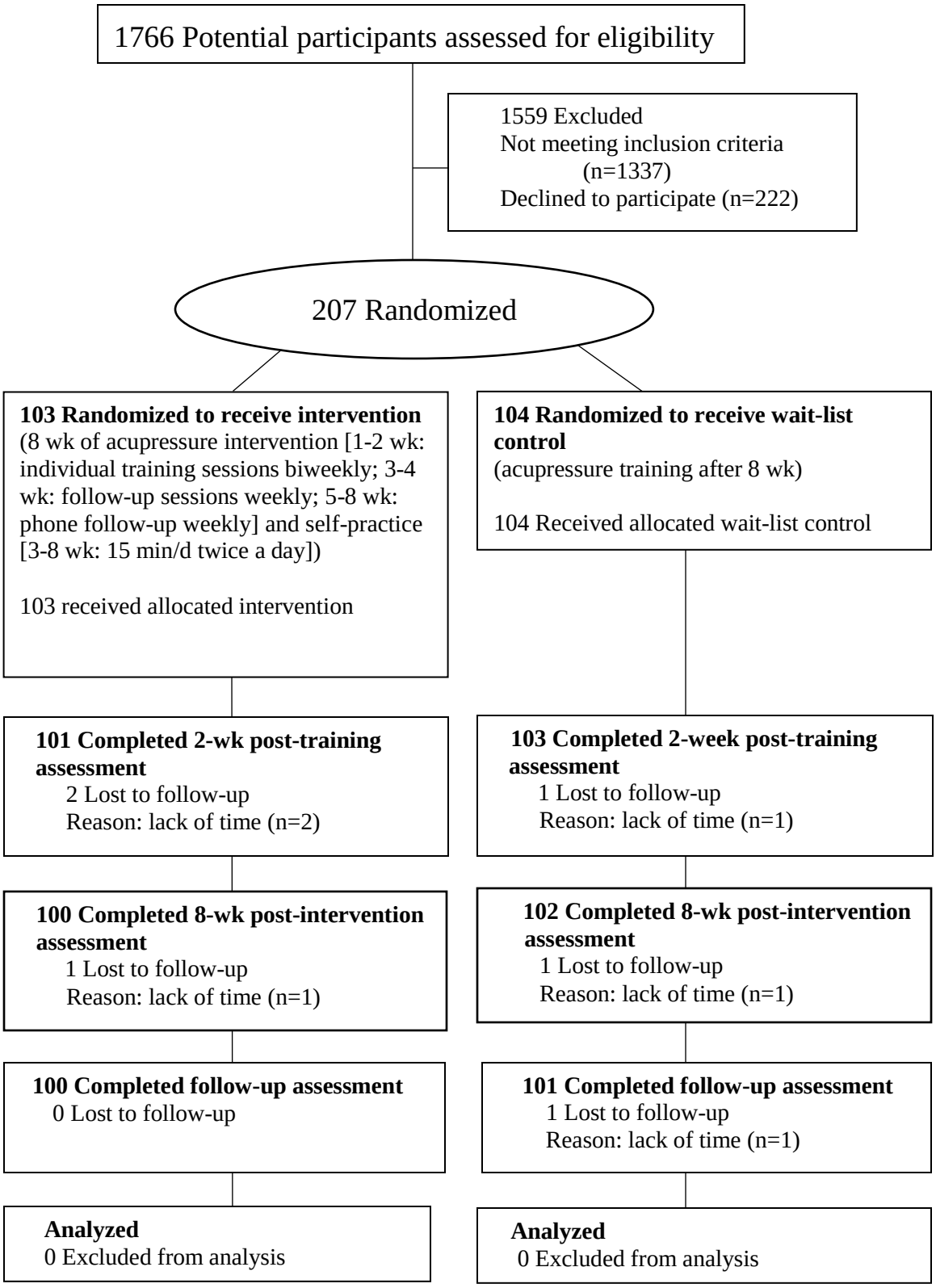
1766 Potential participants assessed for eligibility
1559 Excluded
Not meeting inclusion criteria (n=1337)
Declined to participate (n=222)
207 Randomized
103 Randomized to receive intervention
(8 wk of acupressure intervention [1-2 wk: individual training sessions biweekly; 3-4 wk: follow-up sessions weekly; 5-8 wk: phone follow-up weekly] and self-practice [3-8 wk: 15 min/d twice a day])
103 received allocated intervention
104 Randomized to receive wait-list control
(acupressure training after 8 wk)
104 Received allocated wait-list control
101 Completed 2-wk post-training assessment
2 Lost to follow-up
Reason: lack of time (n=2)
103 Completed 2-week post-training assessment
1 Lost to follow-up
Reason: lack of time (n=1)
100 Completed 8-wk post-intervention assessment
1 Lost to follow-up
Reason: lack of time (n=1)
102 Completed 8-wk post-intervention assessment
1 Lost to follow-up
Reason: lack of time (n=1)
100 Completed follow-up assessment
0 Lost to follow-up
101 Completed follow-up assessment
1 Lost to follow-up
Reason: lack of time (n=1)
Analyzed
0 Excluded from analysis
Analyzed
0 Excluded from analysis

Figure 2