Published in final edited form as:
AIDS Care. 2013 October ; 25(10): 1291–1297. doi:10.1080/09540121.2013.764396.

Effects of behavioral stress reduction Transcendental Meditation intervention in Persons with HIV

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Abstract

Stress is implicated in the pathogenesis and progression of HIV. The Transcendental Meditation is a behavioral stress reduction program that incorporates mind-body approach, and has demonstrated effectiveness in improving outcomes via stress reduction. We evaluated the feasibility of implementing Transcendental Meditation and its effects on outcomes in persons with HIV. In this community based single blinded Phase-I, randomized controlled trial, outcomes (psychological and physiological stress, immune activation, generic and HIV-specific health related quality of life, depression and quality of well-being) were assessed at baseline and at six months, and were compared using parametric and non-parametric tests. Twenty two persons with HIV were equally randomized to Transcendental Meditation intervention or healthy eating (HE) education control group. Retention was 100% in Transcendental Meditation group and 91% in healthy eating control group. The Transcendental Meditation group exhibited significant improvement in vitality. Significant between group differences were observed for generic and HIV-specific health related quality of life.. Small sample size may possibly limit the ability to observe significant differences in some outcomes. Transcendental Meditation stress reduction intervention in community dwelling adults with HIV is viable and can enhance health related quality of life. Further research with large sample and longer follow-up is needed to validate our results.

INTRODUCTION

The number of HIV/AIDS survivors in the U.S. has increased from 168,754 to 487,968 between 1993–2009 (CDC 2012). Improved survival implies that persons with HIV are vulnerable to HIV- specific and non-HIV- specific conditions such as immune activation and impaired wellbeing (Desai S and Landay A 2010; Kovacs A. et al 2010).

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Living with HIV involves facing psychological and physical stressors. Relationship between stress, HIV and health is complex (Bonneau RH. et al 2007; Cohen S. et al 2007; Fumaz C. et al 2009). Studies have explored the association between stress management and psychosocial outcomes in HIV (Robinson F. et al 2003; Carrico AW. et al 2006; Leserman J. 2008). Cortisol is used as a measure of physiological stress (Goodkin K. et al 1996; Ironson G. et al 1996; Cruess DG. et al 2000; Cruess S. et al 2000; Leserman J. et al 2002). Some studies indicate improved immunological function for stress management groups (Antoni MH. et al 1991; Robinson F. et al 2003; Creswell DJ. et al 2009), while others report improvements for intervention and control groups, or no effect (Coates TJ. et al 1989; LaPerriere AR. et al 2009).

Psychoneuroimmunology (PNI) theory provides a framework for analyzing stress-disease relationships (Hand GA. et al 2005). Transcendental Meditation (TM) is a behavioral stress reduction program that incorporates mind-body approach. Studies suggest that TM may improve outcomes across various illnesses (Castillo-Richmond A. et al 2000; Schneider RH. et al 2001; Jayadevappa R. et al 2007; Rainforth MV. et al 2007). Objective of our Phase-I study was to evaluate the feasibility of TM intervention in persons with HIV and analyze the potential effects of stress reduction on psychosocial, hormonal and immunological outcomes.

METHODS

This two arm single blinded randomized control trial (RCT) was approved by the Institutional Review Board. All participants provided written consent. Persons with HIV satisfying following criteria were eligible: age ≥ 18 years; stable on antiretroviral treatment; CD4+ T-Cell count >300 and plasma viral load of <200 copies/ml in the past 6 months; no Hepatitis C, non-diabetic; not on steroids; mini-mental test score of ≥ 25; and not participating in other studies. Intervention group underwent the TM program of six-month duration. Control group underwent a healthy eating (HE) education program of comparable length and structure. We used a community based recruitment initiative. Between April 8 to May 10, 2011, 50 persons contacted the study team, 34 underwent eligibility assessment and 22 were randomized after baseline measurements (Figure 1).

The TM intervention was conducted by a certified instructor and comprised of two phases. Intensive phase consisted of five consecutive sessions of two hours duration each day. Follow-up phase involved bi-weekly sessions for three months, followed by monthly sessions for additional three months. Participants were asked to practice TM twice a day for twenty minutes each over the study period.

The HE education control program was designed to mirror the effects of personal interaction and attention that are part of TM program. This course was conducted by a nurse and addressed more in-depth nutritional information than generally is provided in HIV care. Similar to TM intervention, intensive phase of HE program consisted of five consecutive sessions of two hours duration each day. Follow-up phase involved bi-weekly sessions for three months, followed by monthly sessions for three additional months and were conducted by the same nurse. Participants were asked to engage in an activity, e.g. reading, twice a day for twenty minutes during the study.

Outcomes

Outcomes were assessed at baseline and at six month. We conceptualized feasibility as response to recruitment, and acceptability as study compliance.

Endocrine response was measured by serum norepinephrine and cortisol levels. Blood draws were done between 9–10 am and 25μl of sera were used to quantify Norepinephrine levels (BA E-5200 Rocky Mountain Diagnostics 2012). Cortisol levels were quantified using assay from Parameter Cortisol Assay (R & D Systems 2011). Immune activation was measured by expression of CD38 and HLA-DR on CD4 and CD8 T cells and was analyzed using FlowJo (Treestar 2011).

Perceived Stress Scale (PSS) was used to measure psychological stress (Cohen and Williamson 1988). Generic health related quality of life (HRQoL) was measured using Medical Outcomes Short Form, SF-36 (Ware JE Jr and Sherbourne CD 1992) and HIV-specific HRQoL was measured using Functional Assessment of HIV Infection (FAHI) instrument (Peterman AH. et al 1997). Center for Epidemiological Studies Depression (CESD) scale was used to measure depression (Zich JM. et al 1990). Quality of well-being was measured using Quality of Well-being (QWB-SA) survey (Kaplan RM and Bush]W 1982).

Analysis

Data were analyzed using intent-to-treat approach. We compared distributions of socio-demographic variables between the groups to determine the effectiveness of randomization. Due to small sample size and skewed distribution for some outcomes, we log transformed the outcome scores and performed paired *t* tests for within group changes. For between group effects, changes in scores from baseline to six month were tested using independent *t* tests.

RESULTS

Retention was 100% for TM group and 91% for control group, indicating good feasibility and acceptability of the intervention. Socio-demographic characteristics were comparable between groups (Table 1). Results of within-and-between group analyses are presented in Table 2. At follow-up, perceived stress in TM group was lower than baseline and remained mostly unchanged in the controls. Mean baseline cortisol was comparable between groups. Cortisol was somewhat lower in TM group at follow-up, and higher in the controls. Norepinephrine declined slightly in TM group, and remained unchanged in the control group. While there was no significant difference in level of T cell activation between groups, differences in TM group were closer to zero compared to the controls (Fig2). Additionally, a two part test comparing changes in T cell activation between groups found lower change in HD Effectors CD8+ HLA-DR+ CD38+ freq of CD8+ T cells for TM group (p=0.0633), indicating possibility for immune activation stabilization.

For TM group, SF-36 domains of role emotional, vitality (p=0.0133), mental health, social function and general health showed improvement. General health improved in TM group, and declined in the controls (p=0.0299). Among domains of FAHI, improvement in physical well-being was larger for TM group compared to controls (p=0.0127). Between-group changes were significant for FAHI total score (p=0.0393). Mean CESD score decreased in TM group and remained unchanged in the controls. The QWB improved in TM group, and declined in the controls.

DISCUSSION

In this Phase-I, community based RCT we observed the feasibility and acceptability of TM stress reduction program in persons with HIV. The TM group exhibited significant improvement in generic and HIV-specific HRQoL. We noticed a pattern of improvement in

physiological and psychological parameters in TM group. Some differences were statistically non-significant, possibly due to small sample size and short follow-up.

Research using PNI framework reports benefits of stress reduction in HIV patients (Coates TJ. et al 1989; Antoni MH. et al 1991; Ironson G. et al 1996; McCain NL and Zelle JM 1996; Lutgendorf SK. et al 1997). Stress reduction was associated with reduction in depression (Antoni MH. et al 1991; Lutgendorf SK. et al 1997), anxiety (Ironson G. et al 1996; Lutgendorf SK. et al 1997), improvement in CD4 count (Antoni MH. et al 1991), Natural Killer (NK) cell number (Antoni MH. et al 1991), safer sexual practice (Coates TJ. et al 1989), and emotional well-being (McCain NL and Zelle JM 1996).

Per PNI theory, we conceptualized the pathway where psychosocial/psychological factors are immediately affected by stress. This may be one of the reasons why changes in generic and HIV-specific HRQoL and perceived stress were observed in TM group. Some studies have reported significant effects of stress reduction on cortisol (Ironson G. et al 1996; Cruess DG. et al 2000; Cruess S. et al 2000). However, our results are similar to studies that reported no significant change in cortisol (Leserman J. et al 2002; McCain NL. et al 2003; Robinson F. et al 2003). Reasons for differential findings may be sample size, length of follow-up, type of sample (serum, salivary or urine), time of measurement, and length of HIV-infection.

This is the first study to explore application of TM in community dwelling adults with HIV and adds to the existing evidence regarding association between stress and outcomes. Unique features of our study are RCT design and assessment across all domains of PNI framework. We note following study limitations. Small sample size may possibly limit the ability to observe significant differences in some outcomes. Also, data about mental health treatment or other stress reducing activities of participants was not collected. Finally, those who participated may be more committed to behavior change, leading to self-selection bias.

Increasing numbers of HIV survivors are facing psychological and physical stressors with debilitating effects on health outcomes. Thus, addressing stress reduction in persons with HIV is critical. Our research shows that behavioral stress reduction TM intervention was acceptable in persons with HIV and improved generic and HIV-specific HRQoL. Future research should validate our findings, and help establish TM in particular, and stress reduction in general, as a complementary technique in the battle against HIV.

Acknowledgments

This pilot was funded by the University of Pennsylvania's Center for AIDS Research (CFAR) as part of the Developmental Award Program. We recognize the crucial support and commitment of our study participants. We thank Debora Dunbar, Sara Whittington, Dana Brown, Annet Davis-Vogel, Sheryl Foster, Kevin T. Jones, Chelsea Voytek, Danielle Fiore, Mack Taylor, Pete Smith, Tiffany B. Dominique, Ann Colon, LaRue Rainone and Robert Frederick of HIV Prevention Research Division, University of Pennsylvania; Glenn Davis, Transcendental Meditation instructor; and Julia Bohinski, Health Eating education instructor.

References

Antoni MH, et al. Cognitive-behavioral stress management intervention buffers distress response and immunological changes following notification of HIV-1 seropisitivity. Journal of Consulting and Clinical Psychology. 1991; 59:906–915. [PubMed: 1774375]

BA E–5200 Rocky Mountain Diagnostics. Noradrenaline ELISA kit protocol. Colorado Springs; CO, USA: 2012.

Bonneau RH, et al. Twenty years of psychoneuroimmunology and viral infections in Brain, Behavior, and Immunity. Brain, Behav Immu. 2007; 21:273–280.

Carrico AW, et al. Reductions in depressed mood and denial coping during cognitive behavioral stress management with HIV-positive gay men treated with HAART. Annals of Behavioral Medicine. 2006; 31:155–164. [PubMed: 16542130]

Castillo-Richmond A, et al. Effects of the Transcendental Meditation Program on carotid atherosclerosis in hypertensive African Americans. Stroke. 2000; 31:568–573. [PubMed: 10700487]

CDC. [Accessed August 1, 2012] 2012. http://www.cdc.gov/hiv/resources/factsheets/us.htm

Coates TJ, et al. Stress reduction training changes number of sexual partners but not immune function in men with HIV. American Journal of Public Health. 1989; 79:885–887. [PubMed: 2735479]

Cohen S, et al. Psychological stress and disease. Journal of the American Medical Association. 2007; 298:1685–1687. [PubMed: 17925521]

Creswell DJ, et al. Mindfullness meditation training effects on CD4+ T lymphocytes in HIV-1 infected adults: a small randomized controlled trial. Brain, Behav Immun. 2009; 23:184–188. [PubMed: 18678242]

Cruess DG, et al. Reductions in salivary cortisol are associated with mood improvement during relaxation training among HIV-seropositive men. J Behav Med. 2000; 23:107–122. [PubMed: 10833675]

Cruess S, et al. Reductions in herpes simplex virus type 2 antibody titers after cognitive behavioral stress management and relationships with neuroendocrine function, relaxation skills, and social support in HIV-positive men. Psychosom Med. 2000; 62:828–837. [PubMed: 11139003]

Desai S, Landay A. Early immune senescence in HIV disease. Current HIV/AIDS Reports. 2010; 7:4–10. [PubMed: 20425052]

Fumaz C, et al. Increased peripheral proinflammatory cytokines in HIV-1-infected patients with prolonged viral suppression suffering from high psychological stress. Journal of Acquired Immune Deficiency Syndromes. 2009; 52:427–428. [PubMed: 19858924]

Goodkin K, et al. Bereavement is associated with timedependent decrements in cellular immune function in asymptomatic human immunodeficiency virus type 1-seropositive homosexual men. Clin Diagn Lab Immunol. 1996; 3:109–118. [PubMed: 8770514]

Hand GA, et al. Stress reduction as a means to enhance oral immunity in HIV infected individuals. Journal of the Association of Nurses in AIDS Care. 2005; 16:58–63. [PubMed: 16433110]

Ironson G, et al. Massage therapy is associated with enhancement of the immune system's cytotoxic capacity. Neuroscience. 1996; 84:205–217. [PubMed: 8707483]

Jayadevappa R, et al. Effectiveness of Stress Reduction Program - Randomized Pilot Study. Ethnicity & Disease. 2007; 17:72–77. [PubMed: 17274213]

Kaplan RM, Bush]W. Health-related quality of life measurement for evaluation research and policy analysis. Health Psychology. 1982; 1:61–80.

Kovacs A, et al. Activation of CD8 T cells predicts progression of HIV infection in women co infected with hepatitis C virus. Journal of Infectious Diseases. 2010; 201:823–834. [PubMed: 20151840]

LaPerriere AR, et al. Exercise intervention attenuates emotional distress and natural killer cell decrements following notification of positive serological status for HIV-1. Biofeedback and Self-Regulation. 2009; 15:299–242.

Leserman J. Role of depression, stress and trauma in HIV disease progression. Psychosomatic Medicine. 2008; 70:539–545. [PubMed: 18519880]

Leserman J, et al. Progression to AIDS, a clinical AIDS condition, and mortality: Psychosocial and physiological predictors. Psychol Med. 2002; 32:1059–1073. [PubMed: 12214787]

Lutgendorf SK, et al. Cognitive-behavioral stress management decreases dysphoric mood and herpes simplex virus-type 2 antibody titres in symptomatic gay men. Journal of Consulting and Clinical Psychology. 1997; 65:31–43. [PubMed: 9103732]

McCain NL, Zelle JM. Psychoneuroimmunological studies in HIV disease. Annual Review of Nursing Research. 1996; 14:23–55.

McCain NL, et al. Effects of Stress Management on PNI-Based Outcomes in Persons With HIV Disease. Res Nurs Health. 2003; 26(2):102–117. [PubMed: 12652607]

Peterman AH, et al. Psychometric validation of the revised Functional Assessment of Human Immunodeficiency Virus Infection (FAHI) quality of life instrument. Qual Life Res. 1997; 6:572–584. [PubMed: 9330556]

R & D Systems. ELISA kit KGE-008. Minneapolis; MN, USA: 2011.

Rainforth MV, et al. Stress reduction programs in patients with elevated blood pressure: a systematic review and meta-analysis. Current Hypertension Reports. 2007; 9:520–528. [PubMed: 18350109]

Robinson F, et al. Phycho-Endocrine-Immune responses to Mindfulness-based stress reduction in Individuals infected with the Human Immunodeficiency Virus: A qausi-experimental study. The Journal of Alternative and Complementary Medicine. 2003; 9:683–694. [PubMed: 14629846]

Schneider RH, et al. Behavioral Treatment of Hypertensive Heart Disease in African Americans: Rationale and Design of a RCT. Behav Medicine. 2001; 27:83–95.

Treestar, I. Version 8.8.6. Ashland, OR 97520, USA: Treestart, INC; 2011.

Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36): Conceptual framework and item selection. Med Care. 1992; 30(6):473–483. [PubMed: 1593914]

Zich JM, et al. Screening for depression in primary care clinics: the CES-D and the BDI. Int J Psychiatry Med. 1990; 20:259–277. [PubMed: 2265888]

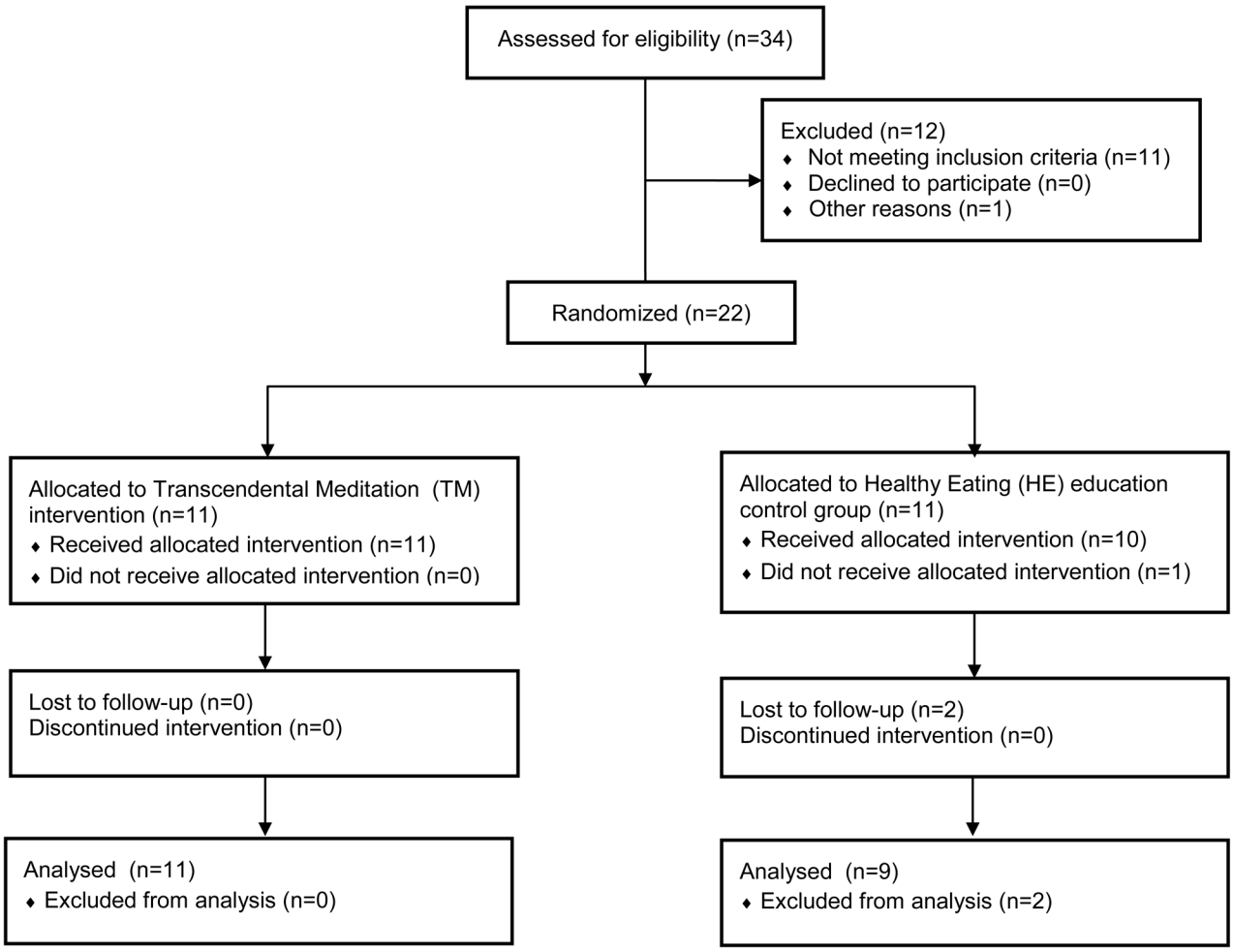

Figure 1.
Recruitment Flow Diagram

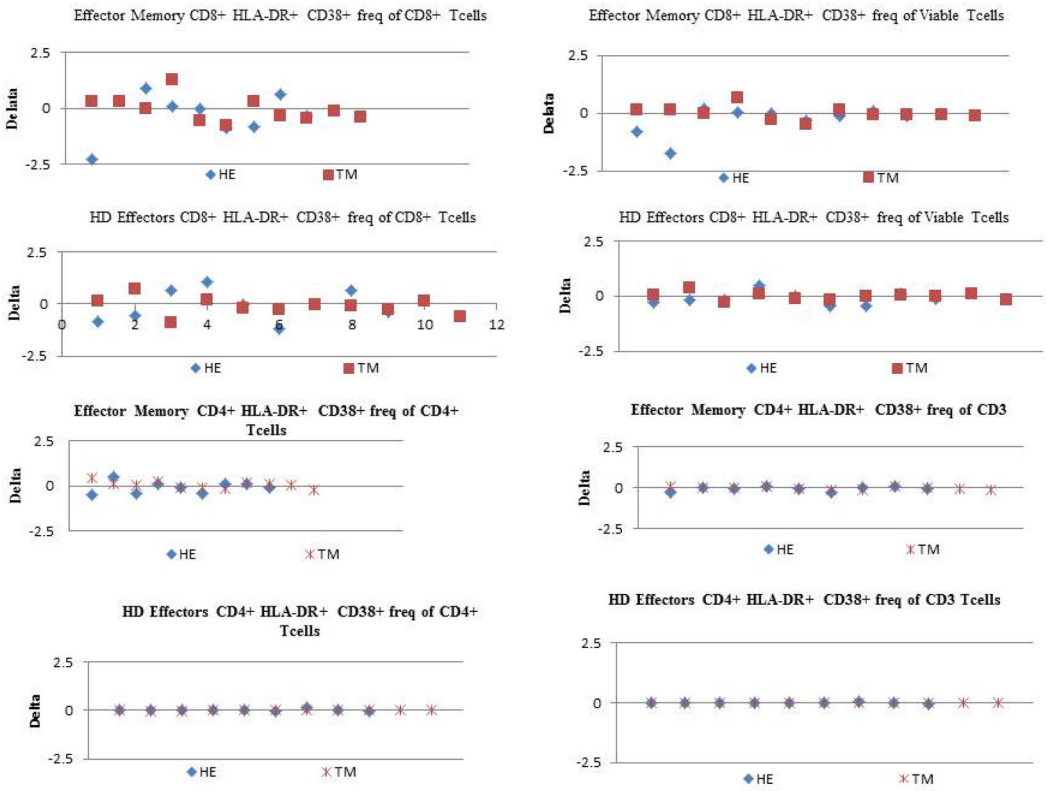

Figure 2.
Change in immune activation markers

Table 1

Demographics of the study population

	Transcendental Meditation (n=11)	Healthy Eating (n=11)
Age in years (mean ± std)	49.7 ± 7.1	50.0 ± 4.4
Gender Male (%)	81.8	81.8
Race (%)		
African American	63.6	81.8
White	9.1	18.2
Hispanic	27.3	0.00
Employment (%)		
Working (Full time/part time)	18.18	27.27
Other (retired, disabled)	81.82	72.73
Ever smoked (%)	54.6	50.00
Length of infection in years (mean ± std)	16.5 ± 6.8	11.2 ± 6.2

AIDS Care. Author manuscript; available in PMC 2014 October 01.

Table 2

Comparison of outcomes

Variable (mean ± standard deviation)	Transcendental Meditation n=11		Healthy Eating Education n=9		Change	
	Baseline	6 month	Baseline	6 month	TM change	HE change
Hormonal outcomes						
Cortisol (ng/ml)	2.36 ± 1.30	2.21 ± 1.65	2.59 ± 1.17	3.01 ± 0.87	0.14±1.17	−0.41±1.89
Norepinephrine (ng/ml)	1.05 ± 0.31	0.91 ± 0.58	0.93 ± 0.20	0.94 ± 0.48	0.13±0.64	−0.01±0.44
Psychological outcomes						
PSS	19.6±3.4	18.4± 5.0	18.6 ±4.9	18.9 ±3.9	1.27±4.3	−0.33±0.61
CESD	18.4 ±9.2	13.5 ± 11.5	19.7 ± 7.7	20.1 ±15.1	4.8±10.8	−0.44±11.7
Health outcomes						
SF-36						
Physical function	60.9±15.14	55.5±24.84	48.3 ± 26.69	41.1 ±23.42	5.45±26.68	7.2±17.52
Role Physical	75.0 ±40.31	70.5 ±41.56	50.0 ± 41.46	33.3 ±33.07	4.55±57.89	16.7±48.41
Role Emotional	72.7 ±41.68	75.8 ± 42.40	62.9 ± 35.14	40.7 ±49.38	−3.03±64.04	22.2±47.14
Vitality	46.0 ±19.42	69.9 ± 19.13*	48.6 ± 25.15	52.8 ±25.98	−23.86±26.78	−4.17±24.41
Mental Health	60.9± 15.14	74.1± 19.98	63.3 ±18.54	71.1± 22.61	−13.18±27.95	−7.78±27.51
Social Function	60.2 ±23.59	73.9± 24.66	63.9 ± 27.56	59.7± 24.03	−13.04±33.75	4.17±30.62
Bodily Pain	75.7 ±24.88	72.0 ± 35.05	57.2 ± 27.85	67.2± 28.32	3.63±34.34	−10.0±21.10
General Health	51.4 ±21.34	66.8 ± 18.48	70.0 ±20.92	63.9± 16.16	−15.45±20.67	6.11±16.16*
FAHI						
Physical well-being	29.2±72.	36.2± 4.2*	28.1 ± 0.23	29.3± 7.9	−7.0.± 6.9	−1.2±4.6
Emotional well-being	28.1±8.9	34.3± 6.0	25.7 ±6.71	25.7± 10.6	−6.8±6.6	0±10.0
Functional and Global well-being	34.6±11.2	38.1± 10.1	34.6 ± 10.26	33.0± 12.1	−3.4±4.8	1.6±5.4
Social well-being	22.4±7.4	23.0± 9.3	18.7± 8.51	18.6± 8.1	−0.63±3.5	0.11±6.7
Cognitive functioning	8.7 ±2.9	9.3 ± 2.9	8.6 ±2.35	7.9 ± 2.8	−0.54±3.2	0.7±3.3
Total Score	123.0 ±28.2	140.8 ± 26.5	115.6± 25.27	114.4 ± 29.1	−17.8±17.9	1.1±19.4*
Quality of well-being	0.69 ± 0.19	0.72 ± 0.22	0.60 ± −.22	0.50 ± 0.19	−0.03±0.27	0.09±0.23

*Significant at p <.05