7-1-2015

Effect of a Mindfulness Intervention on Stress and Coping Strategies in Physician Assistant Students

Mark Volpe

EFFECT OF A MINDFULNESS INTERVENTION ON STRESS AND COPING STRATEGIES IN PHYSICIAN ASSISTANT STUDENTS

A Thesis Presented to
The Faculty of the School of Medicine
Yale University

In Candidacy for the degree of
Master of Medical Science

July 2015

Mark Volpe, MPH, PA-SII
Class of 2015
Yale Physician Associate Program

Signature: _____

Alexandria Garino, MS, PA-C
Assistant Professor
Yale Physician Associate Program
Department of Internal Medicine

Signature: _____

Table of Contents

Abstract

Physician assistant students represent a stressed population, often with poor coping skills. Prior research amongst undergraduate and graduate students has shown that mindfulness interventions are often effective in reducing stress in the short-term. This has not been studied in physician assistant students or for long-term outcomes. We propose a randomized controlled trial to study the effects of a mindfulness intervention on short-term and long-term physician assistant student stress and coping skills. Students from three sites in Connecticut will be provided an eight week mindfulness intervention or be placed in a control group. Stress and coping skills will be measured at baseline, eight weeks, 26 weeks, and 52 weeks to determine intervention effectiveness. This study could offer evidence that mindfulness is an effective means of reducing stress and improving coping skills in both the short and long-term among physician assistant students, which could lead to improved mental health.

Chapter 1: Introduction

Background

Mental illness is the most common cause of disability in the United States, and its resulting disease burden is among the greatest of all diseases. In any given year, 1 in 4 adults suffer from a mental illness and approximately 1 in 17 Americans suffer from a serious mental illness, many of which are preventable. Though most mental illness is believed to be multifactorial, having genetic and environmental components, the most important modifiable risk factor for the development of mental illness is stress.[1] Therefore, interventions aimed at reducing stress, particularly in populations under considerable stress, may help to reduce the risk of developing mental illness in susceptible populations.[2] Physician assistant (PA) students are one of many at-risk populations.[3,4]

The Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-V), defines stress as "the pattern of specific and nonspecific responses a person makes to stimulus events that disturb his or her equilibrium and tax or exceed his or her ability to cope".[5] Coping refers to "conscious effort to solve personal and interpersonal problems, and seeking to master, minimize, or tolerate stress".[6] Stressful situations are often those that are new, unpredictable, uncontrollable, negative, or involve some type of physical or emotional loss. With frequent, high-stakes evaluations, and rapid delivery of curricular content, PA students are exposed to stressful situations on a daily basis.

Ultimately, these situations can directly or indirectly lead to adverse physiological or psychological events. Direct effects of stress include increased blood pressure, increased heart rate, and suppression of the immune system. Stress also acts as a trigger

for mental illness. Indirect effects include increasing risky behaviors such as smoking cigarettes, drinking alcohol, or using illegal substances which then lead to poor health outcomes.[7]

The neurophysiological stress response can be divided into two biologically different components. The first component is the sympathetic fight-or-flight response mediated by the autonomic nervous system. This response to stress involves hypothalamus-induced release of epinephrine and norepinephrine at various neural synapses throughout the body, ultimately resulting in a series of events (Table 1) that prepares the body for metabolic change and movement. These effects are immediate and short-lived (seconds to minutes). Additionally, the hypothalamus stimulates the adrenal medulla through sympathetic preganglionic neurons which results in the release of epinephrine and norepinephrine into the blood stream. This reinforces the sympathetic drive initiated through neural synapses and prolongs the fight-or-flight response (several minutes).[8]

Effects of Activation of the Sympathetic Nervous System
Increased heart rate
Increased myocardial contractility
Vasodilation of skeletal muscle vasculature
Vasoconstriction of smooth muscle vasculature
Pupil dilation
Bronchial dilation
Increased ventilation
Reduced gastrointestinal motility
Reduced genitourinary activity
Glycogenolysis
Gluconeogenesis
Lipolysis

Table 1: Effects of Activation of the Sympathetic Nervous System[8]

The second component of the neurophysiological stress response is the endocrine response to stress, which most prominently involves the adrenal glands. In response to stress, the anterior hypothalamus releases corticotropin-releasing hormone. This stimulates the anterior pituitary to produce and release adrenocorticotropic hormone into the bloodstream. Once adrenocorticotropic hormone reaches the adrenal glands, it stimulates the adrenal cortex to release glucocorticoids such as cortisol (Figure 1). These glucocorticoids then cause several changes in body function (Table 2). These effects can begin in minutes, but often do not fully manifest for days or weeks after the inciting stressor appeared.[8]

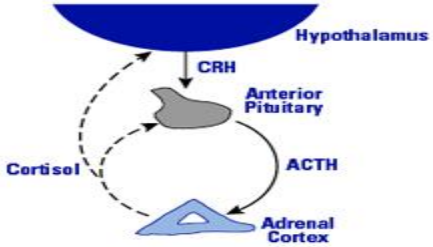

Figure 1: Endocrine Stress Response[9]

Effects of Glucocorticoid Release
Mobilization of free fatty acids
Mobilization of proteins
Metabolizing amino acids
Demineralization of bone
Gluconeogenesis
Weight loss
Muscle wasting
Antibody degradation
Immunosuppression
Vitamin depletion
Beta cell depletion
Decreased insulin production
Increased blood pressure

Table 2: Effects of Glucocorticoid Release[8]

In the short-term, these neurological and endocrine stress responses serve the important function of enabling physical survival in near-death situations. However, the body's response to stress does not distinguish between mental, emotional, and spiritual stress and therefore reacts through the same neurological and endocrine pathways regardless of the type of stress that is experienced. This stress response, which is built for dealing with physical stress, is ineffective in dealing with other types of stress and can be harmful in the long-term. When these responses and pathways are continuously active due to chronic stress, significant damage to the cardiovascular system, digestive system, musculoskeletal system, and immune system can occur. Examples of such damage include tearing of blood vessel endothelium, constipation, gastritis, diarrhea, and hemorrhoids among others.[8]

Furthermore, recent research shows that the areas of the brain that are involved in conscious memory and response to stressful events can also be negatively impacted by chronic stress response activation. The hippocampus, which is involved in forming conscious memories to stressful situations, is rich in cortisol receptors making it particularly sensitive to prolonged cortisol exposure. Repeated exposure to large amounts of cortisol accelerates the aging process of the hippocampus and can even damage or shrink neurons in this area through excess stimulation of corticoid receptors in this region. This leads to decreased length and branching of dendrites, reduced neuroplasticity, increased susceptibility to neurotoxins, and induction of cell death in the hippocampus.[10-12] In addition, the amygdala, which is responsible for the emotional content of our memories (particularly fear), can become hyperexcitable over time due to chronic stress response activation which leads to diminished conduction through a

calcium-activated potassium channel.[13] This diminished conduction has been linked to enhancement of fear conditioning behaviors, which are seen in patients with Post-traumatic Stress Disorder. Additionally, these fear conditioning behaviors have subsided in animal models when conduction through this calcium-activated potassium channel is pharmacologically enhanced.[14,15]

The effects of chronic stress are multiple and affect many systems, including learning, memory, and social well-being. If left unchecked, disease states may develop. Several different stress disorders are identified by the DSM-V. Acute Stress Disorder occurs when an individual experiences exposure to actual or near death, severe injury, or sexual harm and subsequently experiences symptoms of intrusion, dissociation, negative mood, avoidance, and arousal that are new or exacerbated as compared to their levels prior to the inciting event. These symptoms last from three days to one month and cause significant impairment in functioning. Post-traumatic Stress Disorder presents similarly to Acute Stress Disorder, however it lasts longer than one month and can thus cause even more significant functional impairment. Finally, the DSM-V notes that there are Stressor-related Disorders that do not fit into any defined category, but that also cause clinically significant stress and impairment in social, occupational, or other functioning.[5] More extensive definitions for the above mentioned disorders are found in Appendix A.

Stress continues to burden the American population. In general, women report being more stressed than men. However, men report being less concerned about managing stress and are more likely to say that they have their stress under control. Women place more concern on the need to manage stress, but tend to feel that they are not doing well enough. Additionally, stress varies by region. Adults living on the East

Coast of the United States tend to be significantly more stressed and less able to manage the stress than those on the West Coast, Midwest, South, and West. Reasons for this include: those on the East Coast are less willing to take time out of their day to deal with stress, are less likely to report being in excellent health compared to those in other regions, and are more likely to engage in unhealthy behaviors in response to stress. Examples of poor coping strategies used by this segment of the population include skipping meals, overeating, or lying in bed awake in the middle of the night. [16]

In addition to gender and geographic disparities, reported stress levels vary by generation. In a study conducted in 2011, Millennials (18-32 years old), who represent the majority of PA students, reported a stress level of 5.4 on a scale of 1 to 10 with 1 defined as no stress and 10 defined as a great deal of stress. Generation Xers (33-46 years old) reported a stress level of 5.6 on the same scale, while Baby Boomers (47-65 years old) and Matures (age 65 and over) rated their stress at 4.9 and 4.5 respectively. Over the last five years, more than 50% of Millennials and Generation Xers have reported increased stress, while most Baby Boomers report reduced stress. This could be due to older people developing or utilizing better coping strategies or having better aligned expectations for stress as compared to Millennials and Generation Xers. Major contributors to stress among Generation Xers, Millennials, and Baby Boomers are work, money, and housing costs. Among Matures, health concerns are a major cause of stress. Millennials are significantly less stressed about the economy than each of the other generations, and both Millennials and Generation Xers report significantly increased concern about relationships as compared to Baby Boomers and Matures.[16]

The most common causes of stress cited by the American population overall include money, work, the economy, relationships, family responsibility, family health problems, personal health concerns, and housing costs. Many of these also apply to PA students who are often financing their own education, committed in long-distance relationships, finding affordable housing, maintaining certain family responsibilities, and dealing with their own personal health issues. In 2011, 39% of adults reported increased stress from the previous year, and 44% reported increased stress over the five years from 2007 to 2011. Additionally, 53% of Americans reported personal health problems as a result of stress. Importantly, when stress occurs, less than 29% of adults report that they can manage or reduce their stress effectively. Many adults, including PA students, resort to skipping meals, overeating, or reducing sleep in order to cope.[4,16] These unhealthy coping strategies then further perpetuate the stress and can lead to greater disease burden as well as irritability, anhedonia, decreased energy, headaches, gastrointestinal pain, reduced appetite, and reduced sex drive.[16]

Stress management strategies vary among Americans. Appropriate coping strategies include listening to music, exercising or walking, reading, spending time with family and friends, and napping. Interestingly, spending time with family and friends was ranked as one of the most important stress reducers among Americans adults, as 76% and 60% ranked spending time with family and friends respectively as being very important in reducing stress. However, in 2011 only 38% of Americans report utilizing this strategy to reduce their stress.[16] This is down from 46% in 2010.[16,17] Given that PA students often travel to schools far from family and friends to obtain their education, this coping

strategy is even more difficult to utilize and may play a role in increasing stress in this population, as well as facilitating the use of negative coping strategies.

As stress is an unavoidable component of life, it is quite difficult to prevent. However, several strategies can be utilized to reduce the likelihood of stress and make stress easier to manage when it arises. These include identifying stressors and avoiding the controllable ones, setting realistic goals and limits for daily tasks, involving other people more intimately in your daily life, exercising, and becoming more optimistic. By embracing these strategies, individuals can improve their mental health.[18]

One primary prevention technique used to manage stress and prevent further physiological or psychological illness is mindfulness. Mindfulness is a state of active and open attention to the present moment. Thoughts and feelings, rather than being acted on, are observed from a distance and not judged as good, bad, healthy, or unhealthy. Most mindfulness programs utilize a combination of meditation, body awareness, and yoga to help people become more mindful.[19] There are several benefits to practicing mindfulness listed below:

Beneficial Effects of Mindfulness
Increased happiness and contentedness[20-22]
Decreased anxiety, depression, and irritability[23]
Improved memory, reaction times, physical stamina and mental stamina[24-28]
Improved interpersonal relationships[29]
Lowered blood pressure[30]
Reduced impact of chronic diseases such as chronic pain and cancer[31-34]
Assists in relieving drug and alcohol dependence[35]
Strengthened immune system to fight of colds, flu, and other diseases[36]
Associated with increased self-compassion and confidence[37]

Table 3: Beneficial Effects of Mindfulness

There are several advantages to utilizing mindfulness as a stress management coping strategy in addition to the above-mentioned benefits. Mindfulness can be practiced in many settings including at home, on a train, at work, at school or while walking. This makes it convenient. Additionally, mindfulness practice does not take up much time and can be completed in 10-15 minutes each day. This is particularly beneficial for very busy individuals. Also, the focus of mindfulness meditation, body awareness, and yoga is not on success or failure, but rather on the process itself. This means that as long as attempts are made at being mindful, the participant will reap psychological benefits.[19] Furthermore, mindfulness is both accessible and affordable to most individuals. Self-help books teaching mindfulness and providing guided meditation can be purchased for under $20.00.[38] Moreover, there are several free internet based sources for practicing and learning to practice mindfulness.[39]

Finally and most importantly, mindfulness is shown to counter several of the important physiological responses that result from stress. Several studies have shown that mindfulness reduces or normalizes diurnal cortisol secretion which ultimately reduces the stress response and its resulting sequelae.[40-45] Additionally, functional magnetic resonance imaging studies have shown that mindfulness, through neuroplasticity, can increase the density of the hippocampus (the region of the brain associated with self-awareness, compassion, and introspection) and decrease the density of the amygdala (the area of the brain associated with fear and often found to be hyperexcitable in stressed individuals).[46,47] These studies provide a physiological basis for the observed beneficial effects of mindfulness.

Statement of the Problem

Physician assistant (PA) students represent a stressed population due to rigorous class schedules, school time commitment, high expectations of themselves, and high-stakes examination. Such situations provoke stress because they are often new, unpredictable, and out of the student's control. Furthermore, there is often physical or emotional loss that accompanies PA school, such as losing touch with friends, family, or significant others, due to geographic distance and PA school requirements. This too can provoke stress.

One study showed that 39.5% of first year PA students experienced psychological stress between one and two standard deviations above the mean stress level in the general population, while an additional 13.6% of students scored greater than two standard deviations above the mean stress level in the general population.[3] Another study showed that first and second year PA students scored statistically significantly higher (33.3/50) on average than the mean population score (20/50) on the Perceived Stress Scale, meaning that they perceive themselves to be more stressed than the general population. Additionally, 21% of first year PA students (measured in either their first or second semester of study) experienced anxiety between one and two standard deviations above the mean population score, while another 12.3% of students scored greater than two standard deviations above the mean population score. Finally, 28.4% of first year PA students were identified as high risk for meeting the diagnostic criteria for a psychiatric diagnosis.[4] Importantly, there are no studies examining the stress level of PA students prior to program commencement. It is possible that their baseline stress levels may differ from that of the general population.

In addition to PA students being under stress, a perhaps more important and potentially modifiable problem is that students often do not know how to cope with this stress effectively. In one study, 68.6% of first and second year PA students utilized at least one unhealthy coping strategy including self-distraction (distracting yourself from the stressor to avoid having to cope), venting, self-blame, substance abuse, behavioral disengagement, and denial.[4] Though most students also reported using positive coping strategies such as acceptance, active coping, positive reframing and emotional support, it is clear that more can be done to improve coping strategies given the high rate of negative strategy utilization and the high levels of reported stress and anxiety, as well as high-risk for mental illness.

Mindfulness represents one stress management coping strategy that may be effective in the PA student population. Much of the research to date in similar populations, such as other graduate and medical students, suggests that mindfulness therapy may be effective in reducing stress.[48] However, there are also some studies that suggest that it may not be helpful.[49,50] Furthermore, the completed studies examine the short-term effects of mindfulness intervention, and have neither examined the long-term impact that a mindfulness intervention may have on parameters such as stress, nor the short or long-term effects of mindfulness on coping strategies in students. This in itself warrants further investigation.

Moreover and more importantly, the medical student population and curriculum is often quite different from that of PA students, meaning that even if there were clear results either for or against mindfulness in medical students, we likely cannot extrapolate these results to PA students. According to the most recent data, the average medical

student is 24 years old upon matriculation. Also, 47.8% of students are female while 52.2% are male. Caucasians make up just over half of matriculating medical students, and students on average enter with a 3.63 science grade point average (GPA) and 3.69 overall GPA. They receive an average of 776 hours of schooling in their first year, 666 hours in their second year, and require a minimum of 140 weeks to complete their degree over a four-year period, leaving up to 68 weeks for vacation time or other pursuits during their four years.[51] Overall, their curricula involve more in-depth study of core sciences including histology, embryology, and biochemistry, in addition to the anatomy, physiology, pharmacology, and clinical medicine courses shared by PA and medical students.

PA students are older (28.4 years), and less gender and racially diverse (72.7% female; 86.5% Caucasian) than medical students. PA students enter school on average with a 3.36 science GPA, 3.47 overall GPA, and nearly 3,600 hours of direct patient care experience (i.e. emergency medical technician, nurse, medical assistant). They receive an average of 1077 hours of schooling in their didactic curriculum which typically spans 52-64 weeks of the average 114 week program, including an average of eight weeks of vacation.[52] Though the PA curriculum provides less exposure to certain core sciences, it is delivered of a condensed timeframe, making it quite challenging. Clearly, PA and medical students in terms of demographics, working life experience, entering statistics, vacation time during their studies, and curricular experiences are quite different. Thus, it is inappropriate to generalize findings in medical students to PA students, or to assume that medical students and PA students have the same levels of stress, coping skills, or responses to mindfulness.

Therefore, given the lack of mindfulness therapy studies in the PA student population, absence of experimental studies examining long-term outcomes of mindfulness interventions, the need to clarify the effect of mindfulness on professional healthcare students, and the absence of studies examining mindfulness and its relationship to coping skills, there are several gaps to be explored. To fill these gaps in knowledge, this study will examine the effect of a mindfulness intervention on PA students' short and long-term stress and coping skills.

Goals and Objectives

The goal of this study is to examine the effect of a mindfulness intervention on PA students' stress and coping skills. In doing so, this study aims to add to the existing body of literature, examine long-term outcomes, add clarity to the effect of mindfulness on professional healthcare students, and provide specific data regarding a novel population (PA students) and novel effect (mindfulness on overall coping skills). By the end of the study the following objectives will be met:

1. Researchers will understand the perceived stress levels of, and coping skills used, by a sample of PA student participants at baseline, eight weeks, 26 weeks, and 52 weeks post-intervention.
2. Researchers will understand the association between demographic or confounding variables (including age, gender, marital status, highest degree earned, number of months of PA education, hours of class/day, prior meditation practice, and history of care from a mental health provider) and perceived stress, coping skills, and response to a mindfulness intervention.

3. Researchers will determine through statistical analysis the association between mindfulness, stress reduction, and coping skills at eight weeks, 26 weeks, and 52 weeks post-intervention in PA students.

Hypothesis

Primary:

Among PA students, there will be a decrease in stress, as determined by mean change in stress score from baseline, for those participating in an eight-week mindfulness intervention compared to those who do not, at eight weeks, 26 weeks, and 52 weeks post-intervention initiation. Overall stress will be assessed using the Perceived Stress Scale.[53]

Secondary:

Among PA students, there will be a decrease in negative coping skills, as measured by mean change in coping skills score from baseline, for those participating in an eight-week mindfulness intervention compared to those who do not, at eight weeks, 26 weeks, and 52 weeks post-intervention initiation. Overall coping skills will be assessed using the Brief COPE Inventory.[54] We also expect to see a positive correlation between high levels of stress and negative coping skills, as well as between low levels of stress and positive coping skills.

Definitions

Not applicable.

References

1. Reeves WC, Strine TW, Pratt LA, et al. Mental Illness Surveillance Among Adults in the United States. In: Prevention CfDCa, ed. Vol 60. Atlanta, GA: Public Health Surveillance Program Office; 2011:1-32.
2. World Health Organization. *Prevention of Mental Disorders.* Geneva, Switzerland 2004.

3. Childers WA, Jr., May RK, Ball N. An assessment of psychological stress and symptomatology for didactic phase physician assistant students. *The Journal of Physician Assistant Education.*23(4):35-38.
4. O'Brien L, Mathieson K, Leafman J, Rice-Spearman L. Level of stress and common coping strategies among physician assistant students. *The Journal of Physician Assistant Education.*23(4):25-29.
5. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders.* 5 ed. Washington, DC: American Psychiatric Publishing; 2013.
6. Weiten W, Lloyd MA. *Psychology Applied to Modern Life.* Wadsworth: Cengage Learning; 2008.
7. Gelder MG, Andreason NC, Lopez-Ibor JJ, Geddes JR. *New Oxford Textbook of Psychiatry.* Vol 2. New York: Oxford University Press; 2009.
8. Silverthorn DU. *Human Physiology.* 5 ed. San Francisco, CA: Pearson Benjamin Cummings; 2010.
9. Dillman V. The Hypothalamus-Pituitary-Adrenal Axis. Pensacola: The Center for Biogerontology; 1992.
10. McEwen B. *The End of Stress as We Know It.* 1 ed. Washington, D.C.: Joseph Henry Press; 2002.
11. McEwen BS. Stress and hippocampal plasticity. *Annual review of neuroscience.* 1999;22:105-122.
12. Sapolsky RM. Glucocorticoids and hippocampal atrophy in neuropsychiatric disorders. *Archives of general psychiatry.* Oct 2000;57(10):925-935.
13. Rosenkranz JA, Venheim ER, Padival M. Chronic stress causes amygdala hyperexcitability in rodents. *Biological Psychiatry.* 2010;67(12):1128-1136.
14. Atchley D, Hankosky ER, Gasparotto K, Rosenkranz JA. Pharmacological enhancement of calcium-activated potassium channel function reduces the effects of repeated stress on fear memory. *Behavioural brain research.* Jun 15 2012;232(1):37-43.
15. Vick KAt, Guidi M, Stackman RW, Jr. In vivo pharmacological manipulation of small conductance Ca(2+)-activated K(+) channels influences motor behavior, object memory and fear conditioning. *Neuropharmacology.* Mar 2010;58(3):650-659.
16. Anderson NB, Johnson SB, Belar CD, et al. *Stress in America: Our Health at Risk.* Washington, D.C.: American Psychological Association;2012.
17. Anderson NB, Johnson SB, Belar CD, et al. *Stress in America Findings.* Washington, DC: American Psychiatric Association;2010.
18. National Institutes of Health. Stress Affects Both Body and Mind. 2007; http://newsinhealth.nih.gov/2007/January/docs/01features_01.htm. Accessed December 3, 2014.
19. Williams M, Penman D. *Mindfulness.* New York, NY: Rodale; 2011.
20. Ivanovski B, Malhi GS. The psychological and neurophysiological concomitants of mindfulness forms of meditation. *Acta Neuropsychiatrica.* Apr 2007;19(2):76-91.
21. Shapiro SL, Schwartz GE, Bonner G. Effects of mindfulness-based stress reduction on medical and premedical students. *Journal of Behavioral Medicine.* 1998;21(6):581-599.

22. Shapiro SL, Oman D, Thoresen CE, Plante TG, Flinders T. Cultivating mindfulness: effects on well-being. *Journal of Clinical Psychology.* 2008;64(7):840-862.
23. Baer RA, Smith GT, Hopkins J, Krietemeyer J, Toney L. Using self-report assessment methods to explore facets of mindfulness. *Assessment.* 2006;13(1):27-45.
24. Brefczynski-Lewis JA, Lutz A, Schaefer HS, Levinson DB, Davidson RJ. Neural correlates of attentional expertise in long-term meditation practitioners. *Proceedings of the National Academy of Sciences of the United States of America.* 2007;104(27):11483-11488.
25. Jha AP, Krompinger J, Baime MJ. Mindfulness training modifies subsystems of attention. *Cognitive, Affective & Behavioral Neuroscience.* 2007;7(2):109-119.
26. McCracken LM, Yang S-Y. A contextual cognitive-behavioral analysis of rehabilitation workers' health and well-being: Influences of acceptance, mindfulness, and values-based action. *Rehabilitation Psychology.* Nov 2008;53(4):479-485.
27. Ortner CN, Kilner SJ, Zelazo PD. Mindfulness meditation and reduced emotional interference on a cognitive task. *Motivation and Emotion.* Dec 2007;31(4):271-283.
28. Tang YY, Ma Y, Wang J, et al. Short-term meditation training improves attention and self-regulation. *Proceedings of the National Academy of Sciences of the United States of America.* 2007;104(43):17152-17156.
29. Hick S, Segal Z, Bien T. *Mindfulness and the Therapeutic Relationship.* New York, NY: Guilford Press; 2008.
30. Low CA, Stanton AL, Bower JE. Effects of acceptance-oriented versus evaluative emotional processing on heart rate recovery and habituation. *Emotion.* 2008;8(3):419-424.
31. Kabat-Zinn J, Lipworth L, Burncy R, Sellers W. Four-year follow-up of a meditation-based program for the self-regulation of chronic pain: treatment outcomes and complicance. *The Clinical Journal of Pain.* 1986;2(3):159.
32. Morone NE, Greco CM, Weiner DK. Mindfulness meditation for the treatment of chronic low back pain in older adults: a randomized controlled pilot study. *Pain.* 2008;134(3):310-319.
33. Grant JA, Rainville P. Pain sensitivity and analgesic effects of mindful states in Zen meditators: a cross-sectional study. *Psychosomatic Medicine.* 2009;71(1):106-114.
34. Speca M, Carlson LE, Goodey E, Angen M. A randomized, waitlist controlled trial: the effect of a mindfulness meditation-based stress reduction program on mood and symptoms of stress in cancer outpatients. *Psychosomatic Medicine.* 2000;71(1):106-114.
35. Bowen S, Witkiewitz K, Dillworth TM, et al. Mindfulness meditation and substance use in an incarcerated population. *Psychology of addictive behaviors : journal of the Society of Psychologists in Addictive Behaviors.* Sep 2006;20(3):343-347.

36. Davidson RJ, Kabat-Zinn J, Schumacher J, et al. Alterations in brain and immune function produced by mindfulness meditation. *Psychosomatic Medicine.* 2003;65(4):564-570.
37. Olson K, Kemper KJ. Factors associated with well-being and confidence in providing compassionate care. *Journal of evidence-based complementary & alternative medicine.* Oct 2014;19(4):292-296.
38. Amazon. Mindfulness. 2014; http://www.amazon.com/s/ref=nb_sb_noss_1?url=search-alias%3Dstripbooks&field-keywords=mindfulness&sprefix=mindfu%2Cstripbooks. Accessed December 26, 2014.
39. Morgan P. The Free Mindfulness Project. 2014; http://www.freemindfulness.org/download. Accessed December 26, 2014.
40. Jacobs TL, Shaver PR, Epel ES, et al. Self-reported mindfulness and cortisol during a Shamatha meditation retreat. *Health psychology : official journal of the Division of Health Psychology, American Psychological Association.* Oct 2013;32(10):1104-1109.
41. Brand S, Holsboer-Trachsler E, Naranjo JR, Schmidt S. Influence of mindfulness practice on cortisol and sleep in long-term and short-term meditators. *Neuropsychobiology.* 2012;65(3):109-118.
42. Carlson LE, Speca M, Patel KD, Goodey E. Mindfulness-based stress reduction in relation to quality of life, mood, symptoms of stress, and immune parameters in breast and prostate cancer outpatients. *Psychosom Med.* Jul-Aug 2003;65(4):571-581.
43. Carlson LE, Speca M, Faris P, Patel KD. One year pre-post intervention follow-up of psychological, immune, endocrine and blood pressure outcomes of mindfulness-based stress reduction (MBSR) in breast and prostate cancer outpatients. *Brain, behavior, and immunity.* Nov 2007;21(8):1038-1049.
44. Carlson LE, Doll R, Stephen J, et al. Randomized controlled trial of Mindfulness-based cancer recovery versus supportive expressive group therapy for distressed survivors of breast cancer. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology.* Sep 1 2013;31(25):3119-3126.
45. Matousek RH, Dobkin PL, Pruessner J. Cortisol as a marker for improvement in mindfulness-based stress reduction. *Complementary therapies in clinical practice.* Feb 2010;16(1):13-19.
46. Holzel BK, Carmody J, Vangel M, et al. Mindfulness practice leads to increases in regional brain gray matter density. *Psychiatry research.* Jan 30 2011;191(1):36-43.
47. Holzel BK, Carmody J, Evans KC, et al. Stress reduction correlates with structural changes in the amygdala. *Social cognitive and affective neuroscience.* Mar 2010;5(1):11-17.
48. Shiralkar MT, Harris TB, Eddins-Folensbee FF, Coverdale JH. A systematic review of stress-management programs for medical students. *Academic Psychiatry.* 2013;37(3):158-164.
49. Bond AR, Mason HF, Lemaster CM, et al. Embodied health: the effects of a mind-body course for medical students. *Medical Education Online.* 2013;18:1-8.

50. de Vibe M, Solhaug I, Tyssen R, et al. Mindfulness training for stress management: a randomised controlled study of medical and psychology students. *BMC Medical Education.* 2013;13:107.
51. American Association of Medical Colleges. *FACTS: Applicants, Matriculants, Enrollment, Graduates, MD/PhD, and Residency Applicants Data.* Washington DC 2014.
52. Physician Assistant Education Association. *Twenty-Eighth Annual Report: Physician Assistant Educational Programs in the United States.* Washington DC2014.
53. Cohen S, Kamarack T, Mermelstein R. A global measure of perceived stress. *Journal of Health and Social Behavior.* 1983;24:385-396.
54. Carver CS. You want to measure coping but your protocol's too long: Consider the Brief COPE. *International Journal of Behavioral Medicine.* 1997;4:92-100.

Chapter 2: Review of the Literature

Introduction

We reviewed literature through Ovid utilizing the PsycINFO and MEDLINE databases as well as through EBSCO utilizing the Cumulative Index to Nursing and Allied Health Literature (CINAHL) database between August 2014 and June 2015. All articles used were published after 1997 (aside from primary articles describing reliability and validity of instruments used to collect data), and the majority of articles were published in the last five years. A final search was completed on June 13, 2015. Abstracts of articles were reviewed for relevance to the proposed study. Key terms for mindfulness included "mindfulness". To gather articles regarding stress, the category "stress, psychological" was exploded, which included coping. Key terms for students included "students". The three above categories were then combined. Search criteria were narrowed to "English language". Articles used included meta-analyses, systematic reviews, randomized clinical trials, experimental studies, feasibility studies and international articles, as much of the mindfulness research has been conducted abroad.

Scope

This literature review will provide an in depth analysis on prior research completed on mindfulness as it pertains to stress reduction and coping skills in student populations. It will also review studies with anxiety and depression as a primary outcome, as these conditions were likely in part caused by stress. As there have been no studies examining the effect of mindfulness in PA students, studies of other student populations such as medical students, healthcare professional graduate students, and undergraduate students will be reviewed. There is variability in the quality of the studies

in both design and implementation. However, the studies reviewed are similar in that they lack long-term follow-up, measurement of coping strategies, and PA students as the studied population. Overall, there is also room for improvement in our understanding of mindfulness and stress-reduction in the broader student population as there are several studies that support and others that refute the benefits of mindfulness.

Earliest Empirical Studies

The earliest study examining the effects of mindfulness on stress-reduction in medical and premedical students was published in 1998. Shapiro et al. conducted a matched randomized experiment in which 78 participants were assigned to an eight-week mindfulness intervention (a Stress Relaxation and Reduction course) or a wait-list control group. Results found a statistically significant reduction in anxiety in those receiving mindfulness training. Also, as anxiety decreased, depression decreased as well. The wait-list control group then completed the intervention with the same results as the initial intervention group.[1] There were several limitations to this study including lack of assessment of long-term effects of mindfulness beyond the eight-weeks of the intervention, meaning that the long-term effects of such a program are unknown. Additionally, there is an inability to generalize from a population that voluntarily enrolled in the elective course to the larger medical or premedical student population. Finally, there was lack of an alternative intervention to compare the mindfulness intervention to in the comparison group, meaning that any placebo effect that another intervention may have demonstrated was not measured or used for comparison to the treatment group. Thus, further studies were needed to fill these gaps.

In 2003, another study examining the effects of mindfulness on stress reduction in medical students was published by Rosenzweig et al., this time using a different variable called the total mood disturbance which was measured using the Profile of Mood States (POMS) instrument. This instrument includes questions along several axes including tension-anxiety, depression, anger-hostility, vigor-activity, fatigue, and confusion-bewilderment. This was a prospective cohort study of 140 medical students participating in a 10-week mindfulness course and 162 students participating in a complementary medicine course. Students were not randomized and, instead, self-selected the intervention. The total mood disturbance at baseline was significantly higher in the mindfulness group, yet after the 10-week mindfulness intervention, the total mood disturbance was significantly lower in the mindfulness group compared to the complementary medicine group.[2] Limitations in this study include a lack of randomization, which resulted in significant baseline differences between groups, and a difference in the time commitment required of each group. The mindfulness group was assigned homework, but the complementary medicine group was not. This difference in time commitment could have mitigated the effect of the complementary medicine course on the POMS scores and thus contributed to the difference in scores found between treatment and control groups. Groups were not followed beyond 10 weeks.

To address the lack of comparison group in the 1998 article and potential confounding from absence of homework assignments in the comparison group in the 2003 study, as well as the lack of randomization in both studies, a randomized control trial examining mindfulness and its effects on distress and positive state of mind was undertaken by Jain et al. and published in 2007. Eighty-three medical, premedical, and

nursing students were randomized into a mindfulness group, somatic relaxation group, or control group. In comparison with the control group, both the mindfulness and somatic relaxation groups experienced significant decreases in distress and increases in positive mood states over the 4-week intervention. However, there were no differences found between the mindfulness and somatic relaxation groups, suggesting that both are equally effective.[3] Limitations in this study include lack of follow up beyond 10 weeks, minimal generalizability to medical, premedical, or nursing students individually due to mixing the populations to achieve adequate sample size and power (there was also no mention of how many of each type of student were randomized into each group), and the inability to separate the effect of social support and comradery from the effect of the interventions, which were predicated on teamwork rather than simply individual skill practice.

Recent Empirical Studies of Stress

Stress reduction is one of the most studied associations with mindfulness. Several studies with mixed results have identified and proposed different causal pathways associated with mindfulness and stress reduction. These pathways include that stress reduction acts as a mediating variable between mindfulness and a different outcome variable, that mindfulness directly reduces stress, and that mindfulness does not reduce stress in the student population. These studies are reviewed below.

Several studies have identified stress reduction as a mediating variable between mindfulness and another outcome. One cross-sectional study of 553 undergraduate students in 2011 conducted by Roberts et al. found that mindfulness was associated with lower stress, and that lower stress contributed to positive health behaviors and perceptions.[4] Limitations included that observed associations could simply be due to

having a large sample size (making them clinically insignificant), that the cross-sectional nature of the study prevented determination of causal pathways, and that the population was largely white students, limiting the generalizability to the college population, which is more diverse. Another observational study conducted by Caldwell et al. in 2010 found that college students who participated in exercise and movement courses had improved mindfulness, and that stress mediated the relationship.[5] Finally, a 2013 cross-sectional study of college students by Bodenlos et al. found that stress mediated the relationship between mindfulness and alcohol problems.[6] The major limitation to all of these studies was their design. As these were all observational or cross-sectional studies, the causal pathway between the independent and dependent variables could not be determined leaving unanswered the question whether, for example, mindfulness reduced stress which lead to better health behaviors, or whether better health behaviors reduced stress which lead to more mindful thinking.

Mindfulness has been endorsed through systematic reviews to be effective in directly reducing stress and anxiety in medical students.[7] The earliest empirical studies[1-3] provide most of the evidence for this. A recent study conducted in 2009 by Warnecke et al. was a randomized controlled trial carried out at the University of Tasmania to examine this association. Sixty-six medical students were randomized to receive either audio recordings with instruction in mindfulness practice, or nothing as a control group. The intervention lasted eight weeks. Mindfulness was significantly associated with reduced stress and anxiety at both eight and 16 weeks.[8] Strengths of this study included randomization of participants and presence of follow-up beyond the intervention period. Limitations included a small sample size and a control group that did not receive any

comparison intervention which mitigated any placebo effect in comparing the treatment to the control groups.

From these studies, mindfulness appears to be of benefit in reducing stress and anxiety in medical students. However, there are some recent studies that contradict the purported benefit of mindfulness in reducing stress in medical students. A 2013 study of 27 medical students conducted by Bond et al. found that after an 11-week mindfulness course, perceived stress, as measured by the Perceived Stress Scale, was mildly improved without statistical significance.[9] This study was limited by small sample size and lack of a control group. Effect size was not reported.

Another 2013 multi-site international randomized controlled trial of 288 medical and psychology students by de Vibe et al. found that even with this much larger sample size, there was no statistically significant reduced study stress, as measured by the Perceived Medical School Stress scale, in those completing a seven-week mindfulness course. The effect size was Hedge's $g = 0.17$. There was though a moderate reduction in mental distress (effect size of Hedge's $g = 0.65$) measured by the General Health Questionnaire. Significant reductions in study stress were only found when stratifying the results according to gender, with females reporting reduced stress.[10] As other studies have not stratified by gender, there are no other data to compare this to, which may mean that if females do have greater benefit in study stress reduction from mindfulness than males, the proportion of males and females in previously discussed studies may play a larger role in the study outcomes than anticipated. One limitation of the study was that the study randomization was not done by gender, and only 26 males received the intervention. Thus, there were insufficient data to determine the impact of the intervention on male

students (aside from that when combined with female students, no significant differences were found in stress) as the study was not powered for this. Moreover, because students in each tested group interacted with one another during the intervention period, it is possible that control group participants may have participated in the intervention, which would lower the expected effect sizes and may account for the low effect size and absence of statistical significance seen when examining study stress. It is also worth noting that because studies which purport or refute the beneficial effect of mindfulness in this population often utilized different instruments to measure the outcome variable, the results between studies are not easily comparable.

Recent Empirical Studies of Depression and Anxiety

As stress is a known risk factor for both anxiety and depression[11], and mindfulness is purported reduce stress, it is important to understand the effects of mindfulness on anxiety and depression as they may provide further indirect evidence as to the effect of mindfulness on stress in the student population. There have been several studies examining the effect of mindfulness on depression and/or anxiety with largely positive results in individual and meta-analysis.[12] One 2009 cohort study by Hassed et al. at Monash University (Australia) found that medical students enrolled in an integrated mindfulness and lifestyle program had statistically significant reduced depression when measured during the final exam period. Though anxiety was also reduced, it did not achieve statistical significance.[13] Limitations of the study included lack of long-term follow up and lack of a control group. This was the only study with anxiety as a primary outcome where anxiety was not shown to be significantly reduced with a mindfulness intervention. This was likely related to the timing of the data collection around final

exams as the initial data were collected midway through the semester, while the final data were collected in the week that preceded final exams. Importantly, anxiety scores even during the final exam data collection were lower than at baseline, indicating a potential clinically significant reduction in anxiety even though statistical significance at that time point was not reached, possibly due to inadequate power to detect the change (power was not reported).

Another study in 2013 by Barbosa et al. examined the effect of an eight-week mindfulness intervention on anxiety in graduate healthcare students (including podiatric medicine, physical therapy, occupational therapy, and five physician assistant students) and found that there was significant reduction in anxiety at weeks eight and 11.[14] Limitations include a small sample size, lack of control group, and combining of all graduate healthcare students into one group which makes it impossible to determine the effect of mindfulness on each individual healthcare profession's students. Additionally, a prospective cohort study in 2013 found that there were significant reductions in anxiety, depression, and stress in medical students after curricular changes (including a mindfulness component) were made.[15] The major limitation to this study is that the isolated effect of mindfulness on anxiety, depression, and stress could not be determined due to the multiple simultaneous curricular changes that were made.

Furthermore, another study that included a control group has since been completed. In 2013, Cavanagh et al. published a randomized controlled trial using college students and found that anxiety and depressive symptoms were reduced in individuals randomized to undergo a two-week online mindfulness intervention compared to controls.[16] Although this study had a control group, it used an inactive waiting-list control

group meaning that they received no intervention initially and then received the mindfulness intervention after the treatment group completed the intervention. Thus, there was no control of any non-specific effects that could happen just from receiving a control intervention alone, as there was no control intervention. Additionally, the intervention was short and no long term follow-up data were collected beyond the two weeks. Aside from this study, there have been no other studies in the healthcare student population evaluating depression or anxiety as the primary outcome from a mindfulness intervention.

Overall, mindfulness appears to be a successful intervention to reduce stress in undergraduates and other graduate healthcare populations in the short-term. Though there are some studies that refute this, systematic reviews and the most well-designed studies generally support this notion. Similarly, mindfulness appears to be a successful intervention in improving depression and reducing anxiety in graduate healthcare populations in the short-term as well. However, there are no data regarding the effect of mindfulness on PA students, the long-term outcomes related to stress (greater than 16 weeks), or the effect of mindfulness on coping skills.

Review of Relevant Methodology

In addition to reviewing previous study results, it was necessary to review the methodology of studies most relevant to the proposed study, which examines the effect of a mindfulness intervention on stress and coping strategies in PA students. The aim is to review the methods and elements of previous study designs to justify the decisions made in choosing the methodology of the proposed study.

Study Design:

The proposed study will be a randomized controlled trial exploring the effects of mindfulness on stress reduction and coping skills among PA students. This design allows for control of baseline characteristics between the intervention and control groups and is comparable to previous studies of mindfulness in other populations which produced the most valid results.[3,8,10,16] It will not be possible to blind participants given the nature of the intervention; however, every effort will be made to ensure intervention and control groups are similar in terms of time allotted to study-related activities. Also, the primary investigators will be blinded. A research assistant will be responsible for all contact with participants and de-identifying obtained data.

Participant Selection:

A convenience sample of students will be utilized in the proposed study, which is consistent with previous randomized controlled studies.[3,8,10,16] Given the often small accessible study population, this is the most feasible selection method likely to ensure adequate sample size so that a statistically significant change can be detected if one exists. Unlike previous studies, this study will utilize solely PA students as the target population. This will serve as the major inclusion criterion. Several randomized controlled trials did not utilize any exclusion criteria, likely due to sample size concerns.[3,10,16] Given that it will be difficult to separate the effect of the intervention from the effect of mental health care, particularly if it was recently initiated, students who recently began to receive mental health care (specifically psychotherapy, anxiolytics, or anti-depressants initiated in the prior three months) will be excluded from the study population. Students who do not receive mental health care or who have received mental

health care for greater than three months without change to their treatment plan will be included.

Interventions:

Several different mindfulness interventions have been utilized successfully in studies and can generally be divided into two different categories: self-guided interventions and structured course interventions. There were two studies that primarily used self-guided interventions. The study by Cavanagh et al. utilized an online mindfulness intervention that consisted of learning modules about mindfulness as well as daily 10 minute audio mindfulness meditations that were recorded by clinical psychologists. Participants also received reminder emails every three days to encourage them to continue their daily practice.[16] The Warnecke et al. study simply used an audio compact disc of guided mindfulness exercises that was produced specifically for its trial. The compact disc contained 30 minutes of mindfulness recordings that the participants were to follow each day for eight weeks.[8] Both interventions were successful in statistically significantly reducing stress and anxiety. Given the time constraints of a busy PA curriculum, and the success of the above-mentioned self-guided interventions, the most feasible and likely to succeed intervention for the proposed study will be a self-guided intervention (described further in Chapter 3).

The majority of available studies used more structured course interventions of mindfulness. One type of course commonly utilized was an exercise-based course. One study by Caldwell et al. in 2011 used a semester-long college course of Taijiquan, a Chinese martial art, which met twice per week for 50 minutes for a total of 15 weeks. Compared to a control group of students taking a special recreation course, these students

showed statistically significant increases in mindfulness and improvements in stress.[17] Another observational study by Caldwell et al. utilized 15-week college classes in Pilates, Taijiquan, or gyrokinesis as the intervention and also found that mindfulness increased in students participating in any of the three classes.[5] Given the perceived intensive nature and time commitment of these types of exercise courses, it is likely that PA students, particularly those who are stressed and feel that they have little free time, will be less likely to participate. This could create selection bias within the study as students with lower levels of stress may be more likely to participate than those with higher levels of stress. For these reasons, such a course would not be feasible as an intervention in the proposed study.

Another type of course utilized for mindfulness practice was the typical lecture/seminar course with homework assignments. These courses often involved a combination of in-class lecture material on mindfulness, in-class mindfulness practice, homework assignments including using audio cassettes for mindfulness practice, self-practice, or journaling.[1,3,9,10,13,14,18-20] For example, the Rosenzweig et al. prospective cohort study recruited second year medical students to participate in either a 10-week mindfulness seminar or a 10-week complimentary medicine course (control group). The mindfulness seminar consisted of weekly seminars on topics such as body scanning, breath awareness, stretching, listening to your body while eating, meditation while walking, and guided imagery. Additionally, students were given audio cassettes for daily meditation practice and were instructed to practice at home on their own for 20 minutes per day, six days per week utilizing the cassette.[2] Another example intervention included seven 2.5 hour meditation sessions involving sitting, body scanning, and yoga as well as

weekly home practice and journal writing over the eight-week course implemented in the Shapiro et al. study.[1] These types of interventions have also largely been successful in reducing stress. However, once again their intensive nature and time commitment preclude them from being suitable or feasible for PA students given their busy schedule and the lack of extra time in the curriculum for such instruction.

Primary and Secondary Outcomes:

The primary outcome from the proposed study will be the mean change from baseline in self-reported stress. Stress will be measured with the Perceived Stress Scale a reliable and validated tool used to measure the degree to which an individual perceives situations in their life to be stressful.[21] It has been utilized in numerous prior mindfulness studies of students.[5,6,8,9,15-17,22,23] The baseline scores will be used as normative data for comparison to scores at eight weeks, 26 weeks, and 52 weeks post-intervention initiation.

The psychometric properties of the Perceived Stress Scale are adequate, making the instrument appropriate for use in this study. Internal consistency of the scale has been assessed in many studies. A Cronbach's alpha greater than 0.70 is considered the minimum measure of internal consistency; all 12 of the studies that assessed internal consistency of the PSS met this criterion.[24-35] The test-retest reliability was evaluated at intervals of two days to four weeks. In each of several studies, reliability criteria were met.[25,27,33,35] Test-retest reliability beyond four weeks has not been determined.

In addition to reliability, several studies have examined different aspects of the Perceived Stress Scale validity. Construct validity shows that the scale is moderately to strongly correlated with expected variables, such as depression and anxiety, when compared with other valid and reliable instruments[36]. Criterion validity has not been

well-studied for the PSS instrument.[36] This instrument, given its strong overall reliability and construct validity, is appropriate for this project.

The secondary outcome will be the mean change from baseline in coping skills scores as measured by the Brief COPE Inventory, a reliable and validated tool used to evaluate an individual's coping mechanisms.[37] This has been used in the only other study to assess coping strategies in PA students.[38] It has also been used in studies examining coping strategies of burn and cancer patients.[39,40]

Several studies have examined the validity of the Brief COPE Inventory. Construct validity shows correlation between the Brief COPE Inventory and the Perceived Stress Scale, Self-Esteem Inventory, and the 12-item General Health Questionnaire.[37] Positive coping strategies are correlated with reduced stress, improved self-esteem, and low psychological distress while negative coping strategies are correlated with increased stress, low self-esteem, and high psychological distress.

Additionally, several studies have examined the reliability of the Brief COPE Inventory. The internal consistency reliability for each of the 14 different coping dimensions ranges from 0.50 to 0.90 according to one study of survivors of Hurricane Andrew[37], and 0.25 to 1.00 according to another study of women with breast cancer.[40] Despite the wide range in internal consistency, several authors state that the instrument has overall adequate reliability and is an appropriate instrument for examining coping skills.[37,40,41]

Conclusion

Several studies have shown a statistically significant improvement in stress among students in several fields after a mindfulness intervention, while others have

shown no improvement. Regardless of outcome, none of these studies utilized PA students as the major study population, measured coping strategies after the intervention, or assessed long-term follow-up after intervention termination. It is evident then that a randomized controlled trial of adequate sample size is needed to assess the potential benefits of mindfulness in PA students, the potential improvements in stress and coping skills that mindfulness may provide, and the long-term effects of mindfulness interventions on stress and coping skills. Thus, this proposed study will help to fill several gaps in the current literature.

References

1. Shapiro SL, Schwartz GE, Bonner G. Effects of mindfulness-based stress reduction on medical and premedical students. *Journal of Behavioral Medicine.* 1998;21(6):581-599.
2. Rosenzweig S, Reibel DK, Greeson JM, Brainard GC, Hojat M. Mindfulness-based stress reduction lowers psychological distress in medical students. *Teaching & Learning in Medicine.* 2003;15(2):88-92.
3. Jain S, Shapiro SL, Swanick S, et al. A randomized controlled trial of mindfulness meditation versus relaxation training: effects on distress, positive states of mind, rumination, and distraction. *Annals of Behavioral Medicine.* 2007;33(1):11-21.
4. Roberts KC, Danoff-Burg S. Mindfulness and health behaviors: is paying attention good for you? *Journal of American College Health.* 2011;59(3):165-173.
5. Caldwell K, Harrison M, Adams M, Quin RH, Greeson J. Developing mindfulness in college students through movement-based courses: effects on self-regulatory self-efficacy, mood, stress, and sleep quality. *Journal of American College Health.* 2010;58(5):433-442.
6. Bodenlos JS, Noonan M, Wells SY. Mindfulness and alcohol problems in college students: the mediating effects of stress. *Journal of American College Health.* 2013;61(6):371-378.
7. Shiralkar MT, Harris TB, Eddins-Folensbee FF, Coverdale JH. A systematic review of stress-management programs for medical students. *Academic Psychiatry.* 2013;37(3):158-164.
8. Warnecke E, Quinn S, Ogden K, Towle N, Nelson MR. A randomised controlled trial of the effects of mindfulness practice on medical student stress levels. *Medical Education.* 2011;45(4):381-388.
9. Bond AR, Mason HF, Lemaster CM, et al. Embodied health: the effects of a mind-body course for medical students. *Medical Education Online.* 2013;18:1-8.

10. de Vibe M, Solhaug I, Tyssen R, et al. Mindfulness training for stress management: a randomised controlled study of medical and psychology students. *BMC Medical Education.* 2013;13:107.
11. Gelder MG, Andreason NC, Lopez-Ibor JJ, Geddes JR. *New Oxford Textbook of Psychiatry.* Vol 2. New York: Oxford University Press; 2009.
12. Regehr C, Glancy D, Pitts A. Interventions to reduce stress in university students: a review and meta-analysis. *Journal of Affective Disorders.* 2013;148(1):1-11.
13. Hassed C, de Lisle S, Sullivan G, Pier C. Enhancing the health of medical students: outcomes of an integrated mindfulness and lifestyle program. *Advances in Health Sciences Education.* 2009;14(3):387-398.
14. Barbosa P, Raymond G, Zlotnick C, Wilk J, Toomey R, 3rd, Mitchell J, 3rd. Mindfulness-based stress reduction training is associated with greater empathy and reduced anxiety for graduate healthcare students. *Education for Health.* 2013;26(1):9-14.
15. Slavin SJ, Schindler DL, Chibnall JT. Medical student mental health 3.0: improving student wellness through curricular changes. *Academic Medicine.* 2014;89(4):573-577.
16. Cavanagh K, Strauss C, Cicconi F, Griffiths N, Wyper A, Jones F. A randomised controlled trial of a brief online mindfulness-based intervention. *Behaviour Research & Therapy.* 2013;51(9):573-578.
17. Caldwell K, Emery L, Harrison M, Greeson J. Changes in mindfulness, well-being, and sleep quality in college students through taijiquan courses: a cohort control study. *Journal of Alternative & Complementary Medicine.* 2011;17(10):931-938.
18. Kang YS, Choi SY, Ryu E. The effectiveness of a stress coping program based on mindfulness meditation on the stress, anxiety, and depression experienced by nursing students in Korea. *Nurse Education Today.* 2009;29(5):538-543.
19. Astin JA. Stress reduction through mindfulness meditation. Effects on psychological symptomatology, sense of control, and spiritual experiences. *Psychotherapy & Psychosomatics.* 1997;66(2):97-106.
20. Harwani N, Motz K, Graves K, Amri H, Harazduk N, Haramati A. Impact of Changes in Mindfulness on Perceived Stress and Empathy in Medical Students. *The Journal of Alternative and Complimentary Medicine.* 2014;20(5).
21. Cohen S, Kamarack T, Mermelstein R. A global measure of perceived stress. *Journal of Health and Social Behavior.* 1983;24:385-396.
22. Shapiro SL, Brown KW, Thoresen C, Plante TG. The moderation of Mindfulness-based stress reduction effects by trait mindfulness: results from a randomized controlled trial. *Journal of Clinical Psychology.* 2011;67(3):267-277.
23. Ghorbani N, Cunningham CJ, Watson PJ. Comparative analysis of integrative self-knowledge, mindfulness, and private self-consciousness in predicting responses to stress in Iran. *International Journal of Psychology.* 2010;45(2):147-154.
24. Leung DY, Lam TH, Chan SS. Three versions of Perceived Stress Scale: validation in a sample of Chinese cardiac patients who smoke. *BMC public health.* 2010;10:513.

25. Chaaya M, Osman H, Naassan G, Mahfoud Z. Validation of the Arabic version of the Cohen Perceived Stress Scale (PSS-10) among pregnant and postpartum women. *BMC psychiatry.* 2010;10:111.
26. Cohen S, Williamson G. Perceived stress in a probability sample of the United States. Paper presented at: The Social Psychology of Health: Claremont Symposium on Applied Social Sciences1988; Newbury Park, CA.
27. Remor E. Psychometric properties of a European Spanish version of the Perceived Stress Scale (PSS). *The Spanish journal of psychology.* May 2006;9(1):86-93.
28. Roberti JW, Harrington LN, Storch EA. Further Psychometric Support for the 10-Item Version of the Perceived Stress Scale. *Journal of College Counseling.* 2006;9(2):135-147.
29. Mitchell AM, Crane PA, Kim Y. Perceived stress in survivors of suicide: psychometric properties of the Perceived Stress Scale. *Research in nursing & health.* Dec 2008;31(6):576-585.
30. Örücü MÇ, Demir A. Psychometric evaluation of perceived stress scale for Turkish university students. *Stress and Health.* 2009;25(1):103-109.
31. Andreou E, Alexopoulos EC, Lionis C, et al. Perceived Stress Scale: reliability and validity study in Greece. *International journal of environmental research and public health.* Aug 2011;8(8):3287-3298.
32. Wang Z, Chen J, Boyd JE, et al. Psychometric properties of the Chinese version of the Perceived Stress Scale in policewomen. *PloS one.* 2011;6(12):e28610.
33. Reis RS, Hino AA, Anez CR. Perceived stress scale: reliability and validity study in Brazil. *Journal of health psychology.* Jan 2010;15(1):107-114.
34. Lesage FX, Berjot S, Deschamps F. Psychometric properties of the French versions of the Perceived Stress Scale. *International journal of occupational medicine and environmental health.* Jun 2012;25(2):178-184.
35. Wongpakaran N, Wongpakaran T. The Thai version of the PSS-10: An Investigation of its psychometric properties. *BioPsychoSocial medicine.* 2010;4:6.
36. Lee E-H. Review of the Psychometric Evidence of the Perceived Stress Scale. *Asian Nursing Research.*6(4):121-127.
37. Carver CS. You want to measure coping but your protocol's too long: Consider the Brief COPE. *International Journal of Behavioral Medicine.* 1997;4:92-100.
38. O'Brien L, Mathieson K, Leafman J, Rice-Spearman L. Level of stress and common coping strategies among physician assistant students. *The Journal of Physician Assistant Education.*23(4):25-29.
39. Amoyal NR, Mason ST, Gould NF, et al. Measuring coping behavior in patients with major burn injuries: a psychometric evaluation of the BCOPE. *Journal of burn care & research : official publication of the American Burn Association.* May-Jun 2011;32(3):392-398.
40. Yusoff N, Low WY, Yip CH. Reliability and validity of the Brief COPE Scale (English version) among women with breast cancer undergoing treatment of adjuvant chemotherapy: a Malaysian study. *The Medical journal of Malaysia.* Mar 2010;65(1):41-44.
41. Muller L, Spitz E. [Multidimensional assessment of coping: validation of the Brief COPE among French population]. *L'Encephale.* Nov-Dec 2003;29(6):507-518.

Chapter 3: Study Methods

Study Design

We will conduct a multi-centered, randomized controlled trial. The researcher will be blinded to the intervention. Due to the nature of the intervention, the participants will not be blinded.

Study Population and Sampling

Our source population will be derived from the Yale University School of Medicine Physician Associate Program, Quinnipiac University Physician Assistant Program, and University of Bridgeport Physician Assistant Institute located in New Haven, North Haven, and Bridgeport, CT, respectively. A convenience sample of first and second year PA students will be utilized. Inclusion criteria will be full-time enrollment in good standing in one of the three above-mentioned PA programs. Students who recently began to receive mental health care (specifically psychotherapy, anxiolytics, or anti-depressants initiated in the prior three months) will be excluded from the study population. Students who do not receive mental health care or who have received mental health care for greater than three months will be included. All students matching the aforementioned criteria will be approached for recruitment.

In addition to the above inclusion and exclusion criteria, data will be collected to assess confounding and the success of randomization. These data include age, gender, highest degree earned, marital status, number of months of PA education, number of hours of class attended per day, prior meditation practice, baseline Perceived Stress Scale scores, baseline Brief COPE Inventory scores, and history of care received from a mental health provider. The randomization will be used to help control for things such as

progression in the PA program which will vary between the students in the three programs as Yale's program starts in August, Quinnipiac's starts in May, and Bridgeport's starts in January of each year.

Subject Protection and Confidentiality

The application to involve human subjects in biomedical research will be submitted to the Yale Human Research Protection Program's Human Investigation Committee and will be approved prior to initiation of any study-related activities. The required forms will describe the study, study participants, intervention, consent, risks of the study, methods of participant protection, ethics, and timeline of the study. All participants will be over the age of 18 and thus can themselves consent for participation in the proposed study (Appendix B). Any similar forms required by Quinnipiac and the University of Bridgeport will be obtained, completed, and approved prior to initiation of any study-related activities at those campuses.

The research investigators will be required to complete the Health Insurance Portability and Accountability Act training prior to commencement of the study. In addition, they will complete the National Institutes of Health computer-based training program on protecting human research participants. Certificates stating completion of these courses will be provided to the Yale Institutional Review Board as part of the application process.

All information gathered during the study will be stored on a secured, password-protected computer and can only be accessed by researchers requiring direct access to this information. Each researcher will have their own unique user identification name and password to access the computer. Each of the research participants will be given an

alpha-numeric code associated with their data to protect their identity. Any participant identifiers such as name, initials, date of birth, will be destroyed by the research investigators three years after the data are collected, analyzed, and verified per Human Investigations Committee requirements.

Recruitment

All participants will be recruited from the Yale University School of Medicine Physician Associate Program, Quinnipiac University Physician Assistant Program, or the University of Bridgeport Physician Assistant Institute. Recruitment will involve contacting program directors and professors at each institution via email and phone correspondence, and asking them to inform students about the study before or after lectures. Also, time at each of the three programs will be scheduled for investigators to visit the students and explain the project. Additionally, email addresses for currently enrolled students will be obtained via interaction with the program directors, and emails will be sent to all potential participants describing the study and asking for their participation (Appendix D).

All participants will be informed that the goal of the study is to determine the effect of a mindfulness intervention on stress in physician assistant students. They will also be informed that data regarding coping skills will be collected. Additionally, they will be told that their participation will be free of charge and that any required materials will be provided by the investigators. Likewise, participants will not be compensated for their participation. Consent forms will detail that all participants are free to stop participating at any time without any cost to them. We will also reinforce that their institution is not requiring them to complete the study and that their standing in the

program will in no way be affected by their choice to participate or not to participate. The consent form can be found in Appendix B.

Study Variables and Measures

The independent variable in this study will be a mindfulness intervention. The mindfulness intervention will take place over an eight-week period. Participants receiving the intervention at each location will receive an introductory lesson from a community expert lasting for one hour that will consist of an icebreaker, introduction to mindfulness lecture, mindfulness meditation practice, and group discussion. Participants will then be provided with a website where they can access guided mindfulness exercises. They will be instructed to go through one guided exercise each day for the duration of the eight weeks. During the initial lesson, a survey will be completed by each of the participants to gather information regarding the confounding data, in addition to the surveys to determine baseline stress and coping skills scores. These will be completed before the lesson begins and before the topic of mindfulness has been introduced. The control group, rather than receiving a mindfulness intervention, will instead receive a lesson from a community expert on complementary and alternative medicine. Participants in this group will then be instructed to listen to self-selected music for 15 minutes each day for the next eight weeks. They will complete all of the same baseline surveys during their lesson as the intervention group.

The primary dependent variable to be measured in this study is stress. Stress will be assessed using the Perceived Stress Scale. Total stress scores will be determined at baseline, after the eight-week intervention, at 26 weeks post-initiation, and at 52 weeks post-initiation. Both the intervention and control groups will provide data at each of these

time points. The outcome measured will be the mean change in stress score between intervention and control group. At 26 and 52 weeks, an additional question will be added to the survey to assess how often they have been practicing mindfulness since they completed their most recent study survey.

The secondary dependent variable to be measured in this study is coping skills. Coping skills will be assessed using the Brief COPE Inventory. Total coping skills will be determined at baseline, after the eight-week intervention, at 26 weeks post-initiation, and at 52 weeks post-initiation. Both the intervention and control groups will provide data at each of these time points. The outcome measured will be the mean difference in coping skills score between intervention and control groups.

Assignment of Intervention

Each participant will be assigned an alpha-numerical identifier through a random number generator. A computer program will then be used to randomly select identifiers for the intervention and the control group. The research investigators will be blinded to group assignment

Adherence

Each group will receive weekly email reminders from the research assistant. The intervention group will receive an email encouraging them to continue their mindfulness practice on a daily basis. The email will also contain the link to the audio recordings. The control group will receive an email encouraging them to continue to listen to music for 15 minutes each day. Thus, both the intervention and the control group will have equal contact from the research team.

Data Collection

To measure the potential confounding variables, a survey will be administered at the initial lesson for both the treatment and control groups. To measure stress and coping skills the Perceived Stress Scale and Brief COPE Inventory will be entered into an online survey system. Participants will be sent the a link to complete these surveys on day 1 of the intervention and eight weeks, 26 weeks, and 52 weeks post-initiation of the intervention. In each case, the survey will remain open for one week for the participants to complete, and participants will be emailed on the fifth day of each of the survey weeks with a reminder to complete the survey before the end of the week.

Sample Size Calculation

This study will recruit a total of 106 participants (53 per arm) to detect an effect size of 3.4 points and a standard deviation of 6.5 points in the mean change from baseline in the Perceived Stress Scale between intervention and control groups. To estimate the sample size, we used a sample size t-test calculator (Power and Precision, version 4. 2000 Biostat, Inc. Englewood, New Jersey) to compare two independent means for a one-sided alpha of 0.05 and a power of 80%. The sample size estimate also includes a 45% correction of potential attrition during the course of the study. Further information regarding the sample size calculation is located in Appendix E.

Analysis

Data collected during this study will be analyzed using the Statistical Package for the Social Sciences, version 20. From all PA student participants, descriptive statistics will be calculated for the baseline characteristics including age, gender, marital status, highest degree earned, number of months of PA education, hours of class/day, prior

meditation practice, baseline stress score, and history of care from a mental health provider. To compare the means of continuous variables (age, number of months of education, hours of class/day, baseline stress score, baseline coping score), an independent sample t-test will be used. To compare categorical variables (gender, marital status, highest degree earned, prior meditation practice, history of care from a mental health provider), chi-square tests will be used. P-values less than or equal to 0.05 will be considered statistically significant.

To assess the primary outcome of stress, mean scores on the Perceived Stress Scale will be calculated at each of the specified time points (day one, eight weeks, 26 weeks, 52 weeks). The mean difference in stress and coping skills from baseline at each time point for the intervention group will be compared to that of the control group with an independent sample t-test. Additionally, repeated measures analysis of variance (ANOVA) will be performed to compare participant baseline scores with their scores at eight weeks, 26 weeks, and 52 weeks for both the intervention and the control groups. Paired t-tests will be performed if significant differences are detected by the repeated measures ANOVA to determine the comparisons that are statistically significantly different. P-values less than or equal to 0.05 will be considered statistically significant. Intention-to-treat analysis will be used for all comparisons.

To assess the secondary outcome of coping skills, the mean scores on the Brief COPE Inventory will be calculated at each of the specified time points (day one, eight weeks, 26 weeks, 52 weeks). The mean difference in coping skills from baseline at each time point for the intervention group will be compared to those of the control group with an independent sample t-test. Additionally, repeated measures ANOVA will be

performed to compare participant baseline scores with their scores at eight weeks, 26 weeks, and 52 weeks for both the intervention and the control groups. Paired t-tests will be performed if significant differences are detected by the repeated measures ANOVA to determine the comparisons that are statistically significantly different. P-values less than or equal to 0.05 will be considered statistically significant. Intention-to-treat analysis will be used for all comparisons.

If there are significant differences in baseline characteristics of the intervention and control groups after randomization, a regression analysis will be completed in addition to the above-mentioned testing. This would be done to control for confounding differences between groups as measured at baseline.

Timeline and Resources

In keeping with the two year timeframe allowed for this study, the first three months will be dedicated to recruitment activities. The intervention will take another two months, and the following ten months thereafter will be devoted to follow-up and data collection. The remaining time will be designated for statistical analysis and manuscript preparation for publication.

The study will be headquartered at Yale University School of Medicine Physician Associate Program. It is located at 100 Church Street South, Suite A250, New Haven, CT. The study personnel will include the primary investigator, Mark Volpe, M.P.H., PA-S, and the thesis advisor, Alexandria Garino, M.S., PA-C. A dedicated research assistant will be employed to assist with consent, email reminders and data entry, while a biostatistician will be needed to perform the data analysis. There are no other expected personnel requirements.

Additionally, the proposed intervention will require a lecture hall to administer the initial lesson. We will book time with each program at their dedicated lecture halls for their programs to deliver the lesson. The Yale University Qualtrics Survey software will be utilized to administer the surveys. At the research headquarters, a workspace with a computer will be needed for the research assistant to enter data and for the biostatistician to perform data analysis. Additionally, a locked room will be utilized to store data on the secure, password-protected server. A printer, paper, and typical office supplies will also be required.

Chapter 4: Conclusion

Advantages and Disadvantages

The proposed study has several strengths. In being a randomized controlled trial, the assignment of the intervention is the task of the researcher. This increases the probability that the intervention and control groups are similar with respect to known and unknown characteristics and decreases the likelihood of selection bias. Additionally, while mindfulness has been studied in other student populations, this study adds to the body of literature by examining a new population, PA students. Furthermore, this study examines coping skills, a variable never formally examined through mindfulness interventions in students. This study also examines the long-term effect of mindfulness on the primary and secondary outcomes, something that other studies have failed to do.

The study also has some weaknesses. First, participants cannot be blinded to whether they are in the intervention group or control group due to the nature of the intervention. This could introduce information bias, particularly respondent bias, into the study. For example, participants who are assigned the control intervention may be less likely to follow the trial protocol, more likely to seek outside help for reducing stress, or more likely to stop participating in the trial without providing stress or coping skills data. Each of these possibilities could affect the detection of the main outcome. Additionally, while several reminders are in place throughout the course of the study to ensure adherence, the lack of face-to-face interaction may reduce adherence or increase attrition. The sample size that we estimated attempted to account for this. However, this could ultimately result in the need to complete a per-protocol analysis rather than an intention-to-treat analysis if accrual goals are not met. Furthermore, though every attempt has been

made to identify potential confounding variables, any unrecognized confounders could reduce the study validity, though we hope that this will be controlled through randomization.

It is also important to note the potential short-comings of the chosen instruments. The Perceived Stress Scale instrument utilized to evaluate stress has a test-retest reliability that has been proven only up to four weeks. There are no test-retest reliability data beyond that point, meaning that each time point that we measured may only be reflective of the previous four weeks, and not the entire timeframe from the last Perceived Stress Scale administration. Additionally, the Brief COPE inventory has variable test-retest reliability based on each of the tested domains and has only been tested up to eight weeks. Thus, some domains tested may have data that are less reliable than desired, while for those domains that are reliable it is possible that the data are reflective of only the previous eight weeks and not the entire timeframe from the last Brief COPE administration. Further testing is needed to determine the duration of reliability of each of these instruments.

Clinical and/or Public Health Significance

PA students represent a stressed population for various reasons. The psychological stress of PA students is significantly higher than that of the general population, and the coping strategies of PA students are often quite poor.[1] Prior research on mindfulness interventions has targeted different populations of students, has focused on short-term intervention effectiveness, and has not directly measured the effect of mindfulness on coping skills. This study aims to target these gaps in the literature.

If a mindfulness intervention proves effective in reducing stress and improving coping skills among PA students in the short-term and long-term, this treatment could be one that is initiated in this population at the onset of concerning symptoms and could provide benefit for a significant portion of a student's PA education. Furthermore, by reducing stress and improving coping skills, mental illness and worsening symptoms can be prevented which could result in decreased health care costs, reduced absenteeism from school-related activities, and improved quality of life.

References

1. Childers WA, Jr., May RK, Ball N. An assessment of psychological stress and symptomatology for didactic phase physician assistant students. *The Journal of Physician Assistant Education.*23(4):35-38.

Appendices

Appendix A: Diagnostic and Statistical Manual of Mental Disorders, 5th ed., Definitions

Acute Stress Disorder

A. Exposure to actual or threatened death, serious injury, or sexual violation in one (or more) of the following ways:

1. Directly experiencing the traumatic event(s).
2. Witnessing, in person, the event(s) as it occurred to others.
3. Learning that the event(s) occurred to a close family member or close friend. Note: In cases of actual or threatened death of a family member or friend, the event(s) must have been violent or accidental.
4. Experiencing repeated or extreme exposure to aversive details of the traumatic event(s) (e.g., first responders collecting human remains, police officers repeatedly exposed to details of child abuse).

Note: This does not apply to exposure through electronic media, television, movies, or pictures, unless this exposure is work related.

B. Presence of nine (or more) of the following symptoms from any of the five categories of intrusion, negative mood, dissociation, avoidance, and arousal, beginning or worsening after the traumatic event(s) occurred:

Intrusion Symptoms

1. Recurrent, involuntary, and intrusive distressing memories of the traumatic event(s). Note: In children, repetitive play may occur in which themes or aspects of the traumatic event(s) are expressed.
2. Recurrent distressing dreams in which the content and/or affect of the dream are related to the event(s). Note: In children, there may be frightening dreams without recognizable content.
3. Dissociative reactions (e.g., flashbacks) in which the individual feels or acts as if the traumatic event(s) were recurring. (Such reactions may occur on a continuum, with the most extreme expression being a complete loss of awareness of present surroundings.) Note: In children, trauma-specific reenactment may occur in play.
4. Intense or prolonged psychological distress or marked physiological reactions in response to internal or external cues that symbolize or resemble an aspect of the traumatic event(s).

Negative Mood

5. Persistent inability to experience positive emotions (e.g., inability to experience happiness, satisfaction, or loving feelings).

Dissociative Symptoms

6. An altered sense of the reality of one's surroundings or oneself (e.g., seeing oneself from another's perspective, being in a daze, time slowing).
7. Inability to remember an important aspect of the traumatic event(s) (typically due to dissociative amnesia and not to other factors such as head injury, alcohol, or drugs).

Avoidance Symptoms

8. Efforts to avoid distressing memories, thoughts, or feelings about or closely associated with the traumatic event(s).
9. Efforts to avoid external reminders (people, places, conversations, activities, objects,

situations) that arouse distressing memories, thoughts, or feelings about or closely associated with the traumatic event(s).
Arousal Symptoms
10. Sleep disturbance (e.g., difficulty falling or staying asleep, restless sleep).
11. Irritable behavior and angry outbursts (with little or no provocation), typically expressed as verbal or physical aggression toward people or objects.
12. Hypervigilance.
13. Problems with concentration.
14. Exaggerated startle response.
C. Duration of the disturbance (symptoms in Criterion B) is 3 days to 1 month after trauma exposure.
Note: Symptoms typically begin immediately after the trauma, but persistence for at least 3 days and up to a month is needed to meet disorder criteria.
D. The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.
E. The disturbance is not attributable to the physiological effects of a substance (e.g., medication or alcohol) or another medical condition (e.g., mild traumatic brain injury) and is not better explained by brief psychotic disorder.

Posttraumatic Stress Disorder
Note: The following criteria apply to adults, adolescents, and children older than 6 years. For children 6 years and younger, see corresponding criteria below.
A. Exposure to actual or threatened death, serious injury, or sexual violence in one (or more) of the following ways:
1. Directly experiencing the traumatic event(s).
2. Witnessing, in person, the event(s) as it occurred to others.
3. Learning that the traumatic event(s) occurred to a close family member or close friend. In cases of actual or threatened death of a family member or friend, the event(s) must have been violent or accidental.
4. Experiencing repeated or extreme exposure to aversive details of the traumatic event(s) (e.g., first responders collecting human remains: police officers repeatedly exposed to details of child abuse).
Note: Criterion A4 does not apply to exposure through electronic media, television, movies, or pictures, unless this exposure is work related.
B. Presence of one (or more) of the following intrusion symptoms associated with the traumatic event(s), beginning after the traumatic event(s) occurred:
1. Recurrent, involuntary, and intrusive distressing memories of the traumatic event(s).
Note: In children older than 6 years, repetitive play may occur in which themes or aspects of the traumatic event(s) are expressed.
2. Recurrent distressing dreams in which the content and/or affect of the dream are related to the traumatic event(s).
Note: In children, there may be frightening dreams without recognizable content.
3. Dissociative reactions (e.g., flashbacks) in which the individual feels or acts as if the traumatic event(s) were recurring. (Such reactions may occur on a continuum, with the most extreme expression being a complete loss of awareness of present surroundings.)

Note: In children, trauma-specific reenactment may occur in play.
4. Intense or prolonged psychological distress at exposure to internal or external cues that symbolize or resemble an aspect of the traumatic event(s).
5. Marked physiological reactions to internal or external cues that symbolize or resemble an aspect of the traumatic event(s).
C. Persistent avoidance of stimuli associated with the traumatic event(s), beginning after the traumatic event(s) occurred, as evidenced by one or both of the following:
1. Avoidance of or efforts to avoid distressing memories, thoughts, or feelings about or closely associated with the traumatic event(s).
2. Avoidance of or efforts to avoid external reminders (people, places, conversations, activities, objects, situations) that arouse distressing memories, thoughts, or feelings about or closely associated with the traumatic event(s).
D. Negative alterations in cognitions and mood associated with the traumatic event(s), beginning or worsening after the traumatic event(s) occurred, as evidenced by two (or more) of the following:
1. Inability to remember an important aspect of the traumatic event(s) (typically due to dissociative
amnesia and not to other factors such as head injury, alcohol, or drugs).
2. Persistent and exaggerated negative beliefs or expectations about oneself, others, or the world (e.g., "I am bad," "No one can be trusted," 'The world is completely dangerous," "My whole nervous system is permanently ruined").
3. Persistent, distorted cognitions about the cause or consequences of the traumatic event(s) that lead the individual to blame himself/herself or others.
4. Persistent negative emotional state (e.g., fear, horror, anger, guilt, or shame).
5. Markedly diminished interest or participation in significant activities.
6. Feelings of detachment or estrangement from others.
7. Persistent inability to experience positive emotions (e.g., inability to experience happiness, satisfaction, or loving feelings).
E. Marked alterations in arousal and reactivity associated with the traumatic event(s), beginning or worsening after the traumatic event(s) occurred, as evidenced by two (or more) of the following:
1. Irritable behavior and angry outbursts (with little or no provocation) typically expressed as verbal or physical aggression toward people or objects.
2. Reckless or self-destructive behavior.
3. Hypervigilance.
4. Exaggerated startle response.
5. Problems with concentration.
6. Sleep disturbance (e.g., difficulty falling or staying asleep or restless sleep).
F. Duration of the disturbance (Criteria B, C, D, and E) is more than 1 month.
G. The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.
H. The disturbance is not attributable to the physiological effects of a substance (e.g., medication, alcohol) or another medical condition.
Specify whether:

With dissociative symptoms: The individual's symptoms meet the criteria for posttraumatic stress disorder, and in addition, in response to the stressor, the individual experiences persistent or recurrent symptoms of either of the following:
1. Depersonalization: Persistent or recurrent experiences of feeling detached from, and as if one were an outside observer of, one's mental processes or body (e.g., feeling as though one were in a dream; feeling a sense of unreality of self or body or of time moving slowly).
2. Dereaiization: Persistent or recurrent experiences of unreality of surroundings (e.g., the world around the individual is experienced as unreal, dreamlike, distant, or distorted).
Note: To use this subtype, the dissociative symptoms must not be attributable to the physiological effects of a substance (e.g., blackouts, behavior during alcohol intoxication) or another medical condition (e.g., complex partial seizures).
Specify if:
With delayed expression: If the full diagnostic criteria are not met until at least 6 months after the event (although the onset and expression of some symptoms may be immediate).

Other Specified Trauma- and Stressor-Related Disorder
This category applies to presentations in which symptoms characteristic of a trauma- and stressor-related disorder that cause clinically significant distress or impairment in social, occupational, or other important areas of functioning predominate but do not meet the full criteria for any of the disorders in the trauma- and stressor-related disorders diagnostic class. The other specified trauma- and stressor-related disorder category is used in situations in which the clinician chooses to communicate the specific reason that the presentation does not meet the criteria for any specific trauma- and stressor-related disorder. This is done by recording "other specified trauma- and stressor-related disorder" followed by the specific reason (e.g., "persistent complex bereavement disorder"). Examples of presentations that can be specified using the "other specified" designation include the following:
1. Adjustment-like disorders with delayed onset of symptoms that occur more than 3 months after the stressor.
2. Adjustment-like disorders with prolonged duration of more than 6 months without prolonged duration of stressor.
3. Ataque de nervios: See "Glossary of Cultural Concepts of Distress" in the Appendix.
4. Other cultural syndromes: See "Glossary of Cultural Concepts of Distress" in the Appendix.
5. Persistent complex bereavement disorder: This disorder is characterized by severe and persistent grief and mourning reactions (see the chapter "Conditions for Further Study").

Unspecified Trauma- and Stressor-Related Disorder
This category applies to presentations in which symptoms characteristic of a trauma- and stressor-related disorder that cause clinically significant distress or impairment in social, occupational, or other important areas of functioning predominate but do not meet the full criteria for any of the disorders in the trauma- and stressor-related disorders diagnostic

class. The unspecified trauma- or stressor-related disorder category is used in situations in which the clinician chooses not to specify the reason that the criteria are not met for a specific trauma- and stressor-related disorder, and includes presentations in which there is insufficient information to make a more specific diagnosis (e.g., in emergency room settings).

Appendix B: HIC Consent Forms

CONSENT FOR PARTICIPATION IN A RESEARCH PROJECT
YALE UNIVERSITY SCHOOL OF MEDICINE

Study Title: Effect of a Mindfulness Intervention on Stress and Coping Strategies in Physician Assistant Students
Principal Investigator: Mark Volpe, MPH, PA-S
Funding Source: Yale School of Medicine Physician Associate Program

Purpose:

You are invited to participate in a research study that is designed to examine the effects of a mindfulness intervention on stress and coping skills in physician assistant students. You have been asked to participate because you are a physician assistant student at either the Yale University School of Medicine, Quinnipiac University, or the University of Bridgeport, and you may meet the required inclusion and exclusion criteria for the study. Several other physician assistant students in Connecticut will be participating in the study.

To help you decide whether or not you want to participate in this research study, we want to tell you about the risks and benefits of the study so that you can make an informed decision about your participation. This consent will tell you the details about the study which includes its purpose, procedures, risks, and benefits. Once you have read the consent form and understand the study details, we will ask you if you wish to participate. If you do, you will be asked to sign this form to document your consent.

Procedures:

Participation in this study will involve adhering to an eight- week mindfulness intervention which will take approximately 15 minutes per day, or listening to music for 15 minutes per day. Additionally, you will be asked to complete 4 short surveys when you start the study, as well as at eight weeks, 26 weeks, and 52 weeks after the start of the study. The surveys will assess your level of stress and your coping skills.

Risks:

Participants in this study are at minimal risk for any adverse events. Should you begin to experience any significant increase in stress or reduced ability to cope that you believe is related to this study, you are encouraged to discontinue your participation and seek medical care.

Benefits

Although this study may not benefit you personally, this study may provide evidence for a therapeutic modality to reduce stress, anxiety, and depression as well as improve coping skills in physician assistant students.

Confidentiality:

Your participation and your responses to survey questions will be held in strict confidence. Only researchers who are involved in this study and those responsible for overseeing the research will have access to your information. You will be assigned a unique alpha-numerical identifier that will link you with your survey responses, and the list of identifiers for each participant will be stored in a locked file cabinet at the Yale University School of Medicine. However, the investigator can be compelled by a court to disclose this information, unlike a doctor or a lawyer. If the study results are published, there will be no way to identify your information or you as a participant unless we receive your permission to do so. We may also share the data with other researchers to review the accuracy of our conclusions. This will only be done if we are certain that your confidentiality is protected.

Your health information will not be released in any identifiable form outside of the research team, unless required by law. However, your information by be reviewed by the Yale University Human Research Protection Program, Yale University Human Subjects Committee, or the United States Department of Health and Human Services for the purpose of determining that research was conducted in an appropriate fashion. Once the study is completed, any identifying information that we have for our participants will be destroyed after three years.

Voluntary Participation:

Your participation in this study is completely voluntary. You may decline participation or end participation in the study at any time for any reason. You may refuse to answer any study questions that you are uncomfortable answering. If you refuse to participate, you will incur no penalty. By signing this form, you retain all of your legal rights.

Researchers may withdraw you from the study if needed. You may be withdrawn if the intervention you are receiving is causing your stress to worsen to a point where medical attention is needed. If this occurs, treatment will be provided to you, but your insurance company will be required to pay the costs of that treatment.

Questions

If you have any questions about the study, its procedures, purpose, confidentiality, risks or benefits, you can contact the Principal Investigator, Mark Volpe, PA-S at 203-215-4484. If after you have signed this form, you have questions about your privacy rights, you can contact the Yale Privacy Officer at 203-432-5919. If you would like to talk to someone outside of the research team to discuss any concerns about the research, or to discuss something in the if someone from the research team is not available, or to discuss your rights as a participant, please contact the Yale University Human Subjects Committee, Box 208010, New Haven, CT 06520-8010 or at 203-785-4688.

Authorization:

I authorize that I have read (or someone has read to me) the above information, have had the opportunity to have any questions answered about this study, and agree to participate in the study. My signature also indicates that I have received a copy of this consent form.

Name of Participant: _____

Signature: _____

Date: _____

THIS FORM IS VALID ONLY THROUGH: _____ HIC PROTOCOL #: _____ INITIALED: _____

Signature of Principal Investigator _____
Date: _____

Or

Signature of Person Obtaining Consent: _____
Date: _____

Appendix C: Recruitment Materials

EMAIL TO PHYSICIAN ASSISTANT STUDENTS REGARDING INCLUSION IN THE STUDY

Dear PA Student,

We are contacting you about a study that we are conducting regarding mindfulness and its effects on stress and coping skills in physician assistant students. As you likely know, physician assistant students are a potentially stressed population with often poor coping skills. The purpose of this study is to determine if a mindfulness intervention can reduce stress and improving coping skills in physician assistant students. According to information provided to me by your program director, you are a physician assistant student in good standing in your program, and so we are reaching out to you because we would like you to be a part of our study.

Who: Physician assistant students at Yale, Quinnipiac, or the University of Bridgeport, not currently receiving mental health care.

What: Fill out three surveys at the beginning of the study and two surveys again at week eight, 26 and 52 regarding stress and coping skills. Each survey is expected to take 5-10 minutes to complete. Attend one lecture on mindfulness or complementary and alternative medicine. Practice as directed for 10-15 minutes per day on your own schedule.

Study Duration: Eight weeks with follow-up via surveys at 26 weeks and 52 weeks

Compensation: None. However, light refreshments will be served at the introductory lecture.

Contact: If you are interested in participating, please contact the primary investigator by responding to this email so that we can set up a time with your program director for the introductory lecture.

Appendix D: Data Collection Instruments

Demographic Survey

The goal of this project is to determine the effectiveness of a mindfulness intervention on stress reduction and coping skills. You responses will be kept confidential. This survey will take about 5 minutes to complete. Please answer all of the questions to the best of your ability.

1. What is your age? _____

2. What is your gender? _____

3. What is your highest degree earned?

(a)Bachelors (b) Masters (c) Doctorate

4. How many months of your physician assistant program have you completed? _____

5. How many hours of class per weekday do you attend on average? _____

6. Have you ever received care from a mental health provider?

(a) Yes (b) No (c) I don't know

7. Have you ever practiced meditation?

(a) Yes (b) No (c) I don't know

8. Have you initiated any mental health treatment (psychotherapy, anxiety medication, depression medication) in the last 3 months or made any changes to your treatment regimen in the last 3 months?

(a) Yes (b) No (c) I don't know

Perceived Stress Scale

The questions in this scale ask you about your feelings and thoughts during the last month. In each case, you will be asked to indicate by circling how often you felt or thought a certain way.

0 = Never 1 = Almost Never 2 = Sometimes 3 = Fairly Often 4 = Very Often

1. In the last month, how often have you been upset because of something that happened unexpectedly?

0 1 2 3 4

2. In the last month, how often have you felt that you were unable to control the important things in your life?

0 1 2 3 4

3. In the last month, how often have you felt nervous and "stressed"?

0 1 2 3 4

4. In the last month, how often have you felt confident about your ability to handle your personal problems?

0 1 2 3 4

5. In the last month, how often have you felt that things were going your way?

0 1 2 3 4

6. In the last month, how often have you found that you could not cope with all the things that you had to do?

0 1 2 3 4

7. In the last month, how often have you been able to control irritations in your life?

0 1 2 3 4

8. In the last month, how often have you felt that you were on top of things?

0 1 2 3 4

9. In the last month, how often have you been angered because of things that were outside of your control?

0 1 2 3 4

10. In the last month, how often have you felt difficulties were piling up so high that you could not overcome them?

0 1 2 3

Brief COPE

These items deal with ways you've been coping with the stress in your life. There are many ways to try to deal with problems. These items ask what you've been doing to cope with this one (PA school). Obviously, different people deal with things in different ways, but I'm interested in how you've tried to deal with it. Each item says something about a particular way of coping. I want to know to what extent you've been doing what the item says, how much or how frequently. Don't answer on the basis of whether it seems to be working or not—just whether or not you're doing it. Use these response choices. Try to rate each item separately in your mind from the others. Make your answers as true FOR YOU as you can. Write your answer next to each question.

1 = I haven't been doing this at all
2 = I've been doing this a little bit
3 = I've been doing this a medium amount
4 = I've been doing this a lot

1. I've been turning to work or other activities to take my mind off things.
2. I've been concentrating my efforts on doing something about the situation I'm in.
3. I've been saying to myself "this isn't real."
4. I've been using alcohol or other drugs to make myself feel better.
5. I've been getting emotional support from others.
6. I've been giving up trying to deal with it.
7. I've been taking action to try to make the situation better.
8. I've been refusing to believe that it has happened.
9. I've been saying things to let my unpleasant feelings escape.
10. I've been getting help and advice from other people.
11. I've been using alcohol or other drugs to help me get through it.
12. I've been trying to see it in a different light, to make it seem more positive.
13. I've been criticizing myself.

14. I've been trying to come up with a strategy about what to do.
15. I've been getting comfort and understanding from someone.
16. I've been giving up the attempt to cope.
17. I've been looking for something good in what is happening.
18. I've been making jokes about it.
19. I've been doing something to think about it less, such as going to movies, watching TV, reading, daydreaming, sleeping, or shopping.
20. I've been accepting the reality of the fact that it has happened.
21. I've been expressing my negative feelings.
22. I've been trying to find comfort in my religion or spiritual beliefs.
23. I've been trying to get advice or help from other people about what to do.
24. I've been learning to live with it.
25. I've been thinking hard about what steps to take.
26. I've been blaming myself for things that happened.
27. I've been praying or meditating.
28. I've been making fun of the situation.

Appendix E: Sample Size and/or Power Calculation

To estimate the sample size, we used a sample size t-test calculator (Power and Precision version 4. 2000 Biostat, Inc. Englewood, New Jersey) to compare two independent means for a one-sided alpha of 0.05 and a power of 80%.

To detect an effect size of 3.4 points and a standard deviation of 6.5 points in the mean change from baseline in the Perceived Stress Scale, 58 PA students would be needed with 29 in each arm of the study. The assumed effect size represents an expected 22% decline from the assumed baseline Perceived Stress Scale of physician assistant students of 23.3 found by O'Brein et al. (Importantly, this study notes a score of 33.3 for physician assistant students. However, it used a 1 to 5 rating scale instead of a 0 to 4 rating scale as is customary for the Perceived Stress Scale).[1] The 22% expected decline was estimated based on a randomized controlled trial of a mindfulness intervention on medical student stress levels conducted by Warnecke et al.[2] The expected decline in the control arm is 7.5% from the baseline score which was estimated based on a study of college students by Labbe et al. examining the association between different types of music and stress reduction.[3]

Additionally, mindfulness studies have variable attrition rates. Choosing the most conservative estimate of attrition in the reviewed studies, a 45% attrition rate was assumed.[4] Thus an additional 28 patients were needed for each arm to make a total of 106 participants, with 53 in each arm.

References

1. O'Brien L, Mathieson K, Leafman J, Rice-Spearman L. Level of stress and common coping strategies among physician assistant students. *The Journal of Physician Assistant Education.*23(4):25-29.

2. Warnecke E, Quinn S, Ogden K, Towle N, Nelson MR. A randomised controlled trial of the effects of mindfulness practice on medical student stress levels. *Medical Education.* 2011;45(4):381-388.
3. Labbe E, Schmidt N, Babin J, Pharr M. Coping with stress: the effectiveness of different types of music. *Applied psychophysiology and biofeedback.* Dec 2007;32(3-4):163-168.
4. Cavanagh K, Strauss C, Cicconi F, Griffiths N, Wyper A, Jones F. A randomised controlled trial of a brief online mindfulness-based intervention. *Behaviour Research & Therapy.* 2013;51(9):573-578.

Bibliography

1. National Institutes of Health. Stress Affects Both Body and Mind. 2007; http://newsinhealth.nih.gov/2007/January/docs/01features_01.htm. Accessed December 3, 2014.
2. American Association of Medical Colleges. *FACTS: Applicants, Matriculants, Enrollment, Graduates, MD/PhD, and Residency Applicants Data.* Washington DC2014.
3. Amazon. Mindfulness. 2014; http://www.amazon.com/s/ref=nb_sb_noss_1?url=searchalias%3Dstripbooks&field-keywords=mindfulness&sprefix=mindfu%2Cstripbooks. Accessed December 26, 2014.
4. Amoyal NR, Mason ST, Gould NF, et al. Measuring coping behavior in patients with major burn injuries: a psychometric evaluation of the BCOPE. *Journal of burn care & research : official publication of the American Burn Association.* May-Jun 2011;32(3):392-398.
5. Anderson NB, Johnson SB, Belar CD, et al. *Stress in America: Our Health at Risk.* Washington, D.C.: American Psychological Association;2012.
6. Andreou E, Alexopoulos EC, Lionis C, et al. Perceived Stress Scale: reliability and validity study in Greece. *International journal of environmental research and public health.* Aug 2011;8(8):3287-3298.
7. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders.* 5 ed. Washington, DC: American Psychiatric Publishing; 2013.
8. Astin JA. Stress reduction through mindfulness meditation. Effects on psychological symptomatology, sense of control, and spiritual experiences. *Psychotherapy & Psychosomatics.* 1997;66(2):97-106.
9. Atchley D, Hankosky ER, Gasparotto K, Rosenkranz JA. Pharmacological enhancement of calcium-activated potassium channel function reduces the effects of repeated stress on fear memory. *Behavioural brain research.* Jun 15 2012;232(1):37-43.
10. Baer RA, Smith GT, Hopkins J, Krietemeyer J, Toney L. Using self-report assessment methods to explore facets of mindfulness. *Assessment.* 2006;13(1):27-45.
11. Barbosa P, Raymond G, Zlotnick C, Wilk J, Toomey R, 3rd, Mitchell J, 3rd. Mindfulness-based stress reduction training is associated with greater empathy and reduced anxiety for graduate healthcare students. *Education for Health.* 2013;26(1):9-14.
12. Bodenlos JS, Noonan M, Wells SY. Mindfulness and alcohol problems in college students: the mediating effects of stress. *Journal of American College Health.* 2013;61(6):371-378.
13. Bond AR, Mason HF, Lemaster CM, et al. Embodied health: the effects of a mind-body course for medical students. *Medical Education Online.* 2013;18:1-8.
14. Bowen S, Witkiewitz K, Dillworth TM, et al. Mindfulness meditation and substance use in an incarcerated population. *Psychology of addictive behaviors : journal of the Society of Psychologists in Addictive Behaviors.* Sep 2006;20(3):343-347.

15. Brand S, Holsboer-Trachsler E, Naranjo JR, Schmidt S. Influence of mindfulness practice on cortisol and sleep in long-term and short-term meditators. *Neuropsychobiology.* 2012;65(3):109-118.
16. Brefczynski-Lewis JA, Lutz A, Schaefer HS, Levinson DB, Davidson RJ. Neural correlates of attentional expertise in long-term meditation practitioners. *Proceedings of the National Academy of Sciences of the United States of America.* 2007;104(27):11483-11488.
17. Caldwell K, Emery L, Harrison M, Greeson J. Changes in mindfulness, well-being, and sleep quality in college students through taijiquan courses: a cohort control study. *Journal of Alternative & Complementary Medicine.* 2011;17(10):931-938.
18. Caldwell K, Harrison M, Adams M, Quin RH, Greeson J. Developing mindfulness in college students through movement-based courses: effects on self-regulatory self-efficacy, mood, stress, and sleep quality. *Journal of American College Health.* 2010;58(5):433-442.
19. Carlson LE, Doll R, Stephen J, et al. Randomized controlled trial of Mindfulness-based cancer recovery versus supportive expressive group therapy for distressed survivors of breast cancer. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology.* Sep 1 2013;31(25):3119-3126.
20. Carlson LE, Speca M, Faris P, Patel KD. One year pre-post intervention follow-up of psychological, immune, endocrine and blood pressure outcomes of mindfulness-based stress reduction (MBSR) in breast and prostate cancer outpatients. *Brain, behavior, and immunity.* Nov 2007;21(8):1038-1049.
21. Carlson LE, Speca M, Patel KD, Goodey E. Mindfulness-based stress reduction in relation to quality of life, mood, symptoms of stress, and immune parameters in breast and prostate cancer outpatients. *Psychosom Med.* Jul-Aug 2003;65(4):571-581.
22. Carver CS. You want to measure coping but your protocol's too long: Consider the Brief COPE. *International Journal of Behavioral Medicine.* 1997;4:92-100.
23. Cavanagh K, Strauss C, Cicconi F, Griffiths N, Wyper A, Jones F. A randomised controlled trial of a brief online mindfulness-based intervention. *Behaviour Research & Therapy.* 2013;51(9):573-578.
24. Chaaya M, Osman H, Naassan G, Mahfoud Z. Validation of the Arabic version of the Cohen Perceived Stress Scale (PSS-10) among pregnant and postpartum women. *BMC psychiatry.* 2010;10:111.
25. Childers WA, Jr., May RK, Ball N. An assessment of psychological stress and symptomatology for didactic phase physician assistant students. *The Journal of Physician Assistant Education.*23(4):35-38.
26. Cohen S, Kamarack T, Mermelstein R. A global measure of perceived stress. *Journal of Health and Social Behavior.* 1983;24:385-396.
27. Cohen S, Williamson G. Perceived stress in a probability sample of the United States. Paper presented at: The Social Psychology of Health: Claremont Symposium on Applied Social Sciences1988; Newbury Park, CA.
28. Davidson RJ, Kabat-Zinn J, Schumacher J, et al. Alterations in brain and immune function produced by mindfulness meditation. *Psychosomatic Medicine.* 2003;65(4):564-570.

29. de Vibe M, Solhaug I, Tyssen R, et al. Mindfulness training for stress management: a randomised controlled study of medical and psychology students. *BMC Medical Education.* 2013;13:107.
30. Dillman V. The Hypothalamus-Pituitary-Adrenal Axis. Pensacola: The Center for Biogerontology; 1992.
31. Gelder MG, Andreason NC, Lopez-Ibor JJ, Geddes JR. *New Oxford Textbook of Psychiatry.* Vol 2. New York: Oxford University Press; 2009.
32. Ghorbani N, Cunningham CJ, Watson PJ. Comparative analysis of integrative self-knowledge, mindfulness, and private self-consciousness in predicting responses to stress in Iran. *International Journal of Psychology.* 2010;45(2):147-154.
33. Grant JA, Rainville P. Pain sensitivity and analgesic effects of mindful states in Zen meditators: a cross-sectional study. *Psychosomatic Medicine.* 2009;71(1):106-114.
34. Harwani N, Motz K, Graves K, Amri H, Harazduk N, Haramati A. Impact of Changes in Mindfulness on Perceived Stress and Empathy in Medical Students. *The Journal of Alternative and Complimentary Medicine.* 2014;20(5).
35. Hassed C, de Lisle S, Sullivan G, Pier C. Enhancing the health of medical students: outcomes of an integrated mindfulness and lifestyle program. *Advances in Health Sciences Education.* 2009;14(3):387-398.
36. Hick S, Segal Z, Bien T. *Mindfulness and the Therapeutic Relationship.* New York, NY: Guilford Press; 2008.
37. Holzel BK, Carmody J, Evans KC, et al. Stress reduction correlates with structural changes in the amygdala. *Social cognitive and affective neuroscience.* Mar 2010;5(1):11-17.
38. Holzel BK, Carmody J, Vangel M, et al. Mindfulness practice leads to increases in regional brain gray matter density. *Psychiatry research.* Jan 30 2011;191(1):36-43.
39. Ivanovski B, Malhi GS. The psychological and neurophysiological concomitants of mindfulness forms of meditation. *Acta Neuropsychiatrica.* Apr 2007;19(2):76-91.
40. Jacobs TL, Shaver PR, Epel ES, et al. Self-reported mindfulness and cortisol during a Shamatha meditation retreat. *Health psychology : official journal of the Division of Health Psychology, American Psychological Association.* Oct 2013;32(10):1104-1109.
41. Jain S, Shapiro SL, Swanick S, et al. A randomized controlled trial of mindfulness meditation versus relaxation training: effects on distress, positive states of mind, rumination, and distraction. *Annals of Behavioral Medicine.* 2007;33(1):11-21.
42. Jha AP, Krompinger J, Baime MJ. Mindfulness training modifies subsystems of attention. *Cognitive, Affective & Behavioral Neuroscience.* 2007;7(2):109-119.
43. Kabat-Zinn J, Lipworth L, Burncy R, Sellers W. Four-year follow-up of a meditation-based program for the self-regulation of chronic pain: treatment outcomes and complicance. *The Clinical Journal of Pain.* 1986;2(3):159.
44. Kang YS, Choi SY, Ryu E. The effectiveness of a stress coping program based on mindfulness meditation on the stress, anxiety, and depression experienced by nursing students in Korea. *Nurse Education Today.* 2009;29(5):538-543.

45. Klatt M, Kaye G. From Community Need to Classroom Intervention: Fuel for Learning - a Nutrition/Stress Reduction Intervention Delivered Via DVD. *The Journal of Alternative and Complimentary Medicine.* 2014;20(5):Abstract.
46. Kuyken W, Weare K, Ukoumunne OC, et al. Effectiveness of the Mindfulness in Schools Programme: non-randomised controlled feasibility study. *British Journal of Psychiatry.* 2013;203(2):126-131.
47. Labbe E, Schmidt N, Babin J, Pharr M. Coping with stress: the effectiveness of different types of music. *Applied psychophysiology and biofeedback.* Dec 2007;32(3-4):163-168.
48. Lee E-H. Review of the Psychometric Evidence of the Perceived Stress Scale. *Asian Nursing Research.*6(4):121-127.
49. Lesage FX, Berjot S, Deschamps F. Psychometric properties of the French versions of the Perceived Stress Scale. *International journal of occupational medicine and environmental health.* Jun 2012;25(2):178-184.
50. Leung DY, Lam TH, Chan SS. Three versions of Perceived Stress Scale: validation in a sample of Chinese cardiac patients who smoke. *BMC public health.* 2010;10:513.
51. Low CA, Stanton AL, Bower JE. Effects of acceptance-oriented versus evaluative emotional processing on heart rate recovery and habituation. *Emotion.* 2008;8(3):419-424.
52. Matousek RH, Dobkin PL, Pruessner J. Cortisol as a marker for improvement in mindfulness-based stress reduction. *Complementary therapies in clinical practice.* Feb 2010;16(1):13-19.
53. McCracken LM, Yang S-Y. A contextual cognitive-behavioral analysis of rehabilitation workers' health and well-being: Influences of acceptance, mindfulness, and values-based action. *Rehabilitation Psychology.* Nov 2008;53(4):479-485.
54. McEwen B. *The End of Stress as We Know It.* 1 ed. Washington, D.C.: Joseph Henry Press; 2002.
55. McEwen BS. Stress and hippocampal plasticity. *Annual review of neuroscience.* 1999;22:105-122.
56. Mitchell AM, Crane PA, Kim Y. Perceived stress in survivors of suicide: psychometric properties of the Perceived Stress Scale. *Research in nursing & health.* Dec 2008;31(6):576-585.
57. Morgan P. The Free Mindfulness Project. 2014; http://www.freemindfulness.org/download. Accessed December 26, 2014.
58. Morone NE, Greco CM, Weiner DK. Mindfulness meditation for the treatment of chronic low back pain in older adults: a randomized controlled pilot study. *Pain.* 2008;134(3):310-319.
59. Muller L, Spitz E. [Multidimensional assessment of coping: validation of the Brief COPE among French population]. *L'Encephale.* Nov-Dec 2003;29(6):507-518.
60. O'Brien L, Mathieson K, Leafman J, Rice-Spearman L. Level of stress and common coping strategies among physician assistant students. *The Journal of Physician Assistant Education.*23(4):25-29.
61. Olson K, Kemper KJ. Factors associated with well-being and confidence in

providing compassionate care. *Journal of evidence-based complementary & alternative medicine.* Oct 2014;19(4):292-296.
62. Organization WH. *Prevention of Mental Disorders.* Geneva, Switzerland2004.
63. Ortner CN, Kilner SJ, Zelazo PD. Mindfulness meditation and reduced emotional interference on a cognitive task. *Motivation and Emotion.* Dec 2007;31(4):271-283.
64. Örücü MÇ, Demir A. Psychometric evaluation of perceived stress scale for Turkish university students. *Stress and Health.* 2009;25(1):103-109.
65. Physician Assistant Education Association. *Twenty-Eighth Annual Report: Physician Assistant Educational Programs in the United States.* Washington DC2014.
66. Reeves WC, Strine TW, Pratt LA, et al. Mental Illness Surveillance Among Adults in the United States. In: Prevention CfDCa, ed. Vol 60. Atlanta, GA: Public Health Surveillance Program Office; 2011:1-32.
67. Regehr C, Glancy D, Pitts A. Interventions to reduce stress in university students: a review and meta-analysis. *Journal of Affective Disorders.* 2013;148(1):1-11.
68. Reis RS, Hino AA, Anez CR. Perceived stress scale: reliability and validity study in Brazil. *Journal of health psychology.* Jan 2010;15(1):107-114.
69. Remor E. Psychometric properties of a European Spanish version of the Perceived Stress Scale (PSS). *The Spanish journal of psychology.* May 2006;9(1):86-93.
70. Roberti JW, Harrington LN, Storch EA. Further Psychometric Support for the 10-Item Version of the Perceived Stress Scale. *Journal of College Counseling.* 2006;9(2):135-147.
71. Roberts KC, Danoff-Burg S. Mindfulness and health behaviors: is paying attention good for you? *Journal of American College Health.* 2011;59(3):165-173.
72. Rosenkranz JA, Venheim ER, Padival M. Chronic stress causes amygdala hyperexcitability in rodents. *Biological Psychiatry.* 2010;67(12):1128-1136.
73. Rosenzweig S, Reibel DK, Greeson JM, Brainard GC, Hojat M. Mindfulness-based stress reduction lowers psychological distress in medical students. *Teaching & Learning in Medicine.* 2003;15(2):88-92.
74. Sapolsky RM. Glucocorticoids and hippocampal atrophy in neuropsychiatric disorders. *Archives of general psychiatry.* Oct 2000;57(10):925-935.
75. Shapiro SL, Brown KW, Thoresen C, Plante TG. The moderation of Mindfulness-based stress reduction effects by trait mindfulness: results from a randomized controlled trial. *Journal of Clinical Psychology.* 2011;67(3):267-277.
76. Shapiro SL, Oman D, Thoresen CE, Plante TG, Flinders T. Cultivating mindfulness: effects on well-being. *Journal of Clinical Psychology.* 2008;64(7):840-862.
77. Shapiro SL, Schwartz GE, Bonner G. Effects of mindfulness-based stress reduction on medical and premedical students. *Journal of Behavioral Medicine.* 1998;21(6):581-599.
78. Shiralkar MT, Harris TB, Eddins-Folensbee FF, Coverdale JH. A systematic review of stress-management programs for medical students. *Academic Psychiatry.* 2013;37(3):158-164.
79. Silverthorn DU. *Human Physiology.* 5 ed. San Francisco, CA: Pearson Benjamin

Cummings; 2010.
80. Slavin SJ, Schindler DL, Chibnall JT. Medical student mental health 3.0: improving student wellness through curricular changes. *Academic Medicine.* 2014;89(4):573-577.
81. Speca M, Carlson LE, Goodey E, Angen M. A randomized, waitlist controlled trial: the effect of a mindfulness meditation-based stress reduction program on mood and symptoms of stress in cancer outpatients. *Psychosomatic Medicine.* 2000;71(1):106-114.
82. Tang YY, Ma Y, Wang J, et al. Short-term meditation training improves attention and self-regulation. *Proceedings of the National Academy of Sciences of the United States of America.* 2007;104(43):17152-17156.
83. Vick KAt, Guidi M, Stackman RW, Jr. In vivo pharmacological manipulation of small conductance Ca(2+)-activated K(+) channels influences motor behavior, object memory and fear conditioning. *Neuropharmacology.* Mar 2010;58(3):650-659.
84. Wall RB. Tai Chi and mindfulness-based stress reduction in a Boston Public Middle School. *Journal of Pediatric Health Care.* 2005;19(4):230-237.
85. Wang Z, Chen J, Boyd JE, et al. Psychometric properties of the Chinese version of the Perceived Stress Scale in policewomen. *PloS one.* 2011;6(12):e28610.
86. Warnecke E, Quinn S, Ogden K, Towle N, Nelson MR. A randomised controlled trial of the effects of mindfulness practice on medical student stress levels. *Medical Education.* 2011;45(4):381-388.
87. Weiten W, Lloyd MA. *Psychology Applied to Modern Life.* Wadsworth: Cengage Learning; 2008.
88. Williams M, Penman D. *Mindfulness.* New York, NY: Rodale; 2011.
89. Wongpakaran N, Wongpakaran T. The Thai version of the PSS-10: An Investigation of its psychometric properties. *BioPsychoSocial medicine.* 2010;4:6.
90. Yusoff N, Low WY, Yip CH. Reliability and validity of the Brief COPE Scale (English version) among women with breast cancer undergoing treatment of adjuvant chemotherapy: a Malaysian study. *The Medical journal of Malaysia.* Mar 2010;65(1):41-44.