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A Randomized Trial of Differential Effectiveness of Service Dog Pairing Versus Emotional Support Dog Pairing to Improve Quality of Life for Veterans with PTSD

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Abstract

Objectives. Determine whether overall disability and quality of life of Veteran participants in treatment for PTSD are improved by the provision of service dogs relative to provision of emotional support dogs.

Design. Multicenter parallel, two-arm, randomized clinical trial with Veteran participants diagnosed with PTSD assigned 1:1 to either a service dog or an emotional support dog. Randomization was conducted centrally by the study coordinating center using the computer-generated Interactive Touch Tone Randomization System (ITTRS).

Setting. Three VA medical centers: Atlanta VA Medical Center (Atlanta, GA) Iowa City Veterans Affairs Health Care System (Iowa City, IA), and VA Portland Health Care System (Portland, OR).

Participants. 227 Veteran participants were randomized and fulfilled study requirements, of which 181 were paired with a study dog.

Intervention. After randomization to either the service dog intervention or emotional support dog intervention, an observation period of at least three months duration began; during this period both the study team and the participants were blinded to the type of dog to which the participant had been randomized. Dog type assignment disclosure to the participant and the study team occurred upon completion of the observation period. Participants were paired with either service dogs or emotional support dogs per assignment and followed for 18 months.

Main outcome measures. Overall disability (WHO-DAS 2.0) and quality of life (VR-12). Secondary outcomes included PTSD symptoms (PCL-5), suicidal ideation (C-SSRS), depression (PHQ-9), sleep (PSQI) and anger (DAR).

Results. 227 participants were randomized to either the service dog intervention (n=114) or emotional support dog (n=113) intervention. 46 participants terminated prior to pairing; (n=17) participants assigned to the service dog intervention versus (n=29) participants assigned to the emotional support dog intervention. 97 participants were paired with a service dog; 84 participants were paired with an emotional support dog. 9 participants paired with a service dog terminated after pairing; 19 participants paired with an emotional support dog terminated after pairing. Participants paired with a dog were on average 50.6 years old (SD=13.6; range 22-79), mostly male (80.1%), white (66.3%), and non-Hispanic (91.2%). After adjusting for baseline score, center, and gender, the linear mixed repeated measures (LMRM) model for WHO-DAS 2.0 (disability) showed no statistical difference between the two intervention groups nor did the mixed models for quality of life (VR-12) show statistical differences between the two groups for either PCS (physical health) or MCS (mental health). Of the secondary outcome measures, only PCL-5 (PTSD symptoms) using the adjusted LRMR model showed a statistically significant difference between intervention groups. Participants receiving the service dog intervention had a 3.7-point improvement (lower score=less symptoms of PTSD) in the PCL-5 total score over time as compared to the emotional dog intervention. Contrasts testing for a difference in the service dog group versus the emotional support dog group for suicidal ideation and behavior (per C-SSRS) did not show a significant difference between groups across time, however, it did show a difference between groups at 18 months with the service dog group having fewer suicidal behaviors and ideation. In both groups, WHO-DAS 2.0

scores at 18 months decreased (less disability) from scores at 3 months post pairing; improvement in VR-12 MCS also showed some improvement over time in both groups. Descriptive statistics for sleep and anger also showed a decline in scores (improvement) over time in both groups. Serious Adverse Events (SAE) and adverse events (AE) were compared across groups. None of the SAEs in either group were dog related. All AEs occurred in the emotional support dog group.

Conclusions. While both groups appeared to have experienced some benefit, an improvement in overall disability and quality of life among Veteran participants with PTSD was not observed with the provision of a service dog relative to provision of an emotional support dog. Among secondary outcome measures, participants paired with a service dog experienced a reduction in the severity of PTSD symptoms (PCL-5) compared to participants paired with an emotional support dog, and had fewer suicidal behaviors and ideations, particularly at 18 months post-pairing.

Trial registration. This clinical trial was registered at ClinicalTrials.gov, #NCT02039843.

Funding. Funding for this study was provided by the Department of Veterans Affairs.

Glossary of Selected Terms

Baseline assessments – those assessments (Baseline 1) collected before randomization to dog type (service dog or emotional support dog); occurred mostly at the participant's home, but some occurred at the clinic screening visit.

Benefit – as defined for this study, an advantage or an improvement gained, which for study design reasons, may or may not be directly attributable to the intervention of a service dog as compared to an emotional support dog.

Central Leadership Team - consisted of the Study Chair, Coordinating Center team, Executive Committee and the VA Chief Veterinary Medical Officer. This team was responsible for making study protocol-related and dog-related decisions and for managing and analyzing data.

Clearing/Cleared Assessments - assessments at clearing refer to those assessments (Baseline 2) collected after randomization but before pairing (Note: There is a clinic clearing visit and a home clearing visit, but assessments related to study outcomes were collected at the clinic clearing visit).

Cleared - completion of the clearing process.

Clinical Trial – a research study in which human participants are prospectively assigned to one or more health-related interventions to determine the effects on health outcomes. For the purpose of this monograph, the terms clinical trial and study may be used interchangeably.

Clinician Administered PTSD Scale (CAPS) – a structured clinical interview administered by a trained interviewer to assess the essential features of PTSD. Also known as CAPS-5.

Coordinating Center Team - consisted of a study biostatistician, project manager, statistical programmer, database programmer, and other support personnel; this team is responsible for administrative tasks, data processing, and statistical support for the study.

Emotional Support Dog- a dog trained in obedience commands but not trained to perform a task that mitigates a disability per the Americans with Disabilities Act (ADA); therefore, emotional support dogs are not service dogs. Emotional support dogs have some legal protections in housing and air travel but are not given legal rights to be present in public spaces by the ADA like service dogs. This dog type is sometimes abbreviated "EMOT" in this report (see related definition for "service dog" below).

Executive Committee - the management and decision-making body for the operational aspects of the study.

Handler - denotes a participant who has learned or was in the process of learning to give commands to either a service dog or an emotional support dog.

Institutional Animal Care and Use Committee – a specially constituted committee charged with ensuring the humane care and use of animals used in research and teaching.

Institutional Review Board – a specially constituted committee charged with ensuring that studies involving humans are ethical and fair.

Intervention – the treatment or some of provision of care that is being investigated for which the outcome measures have been defined.

Local Study Team (one per study site) - the team was responsible for local data collection. Membership at each site consisted of the site study investigator, a study coordinator, a research assistant, and two dog trainers.

Local VA Dog Trainer (two per study site) – an individual employed by the VA with special skills and knowledge about training dogs. Each VA research site had Local VA Dog Trainers

assigned to assist the participants at that site with any problems they experienced after they received either a service dog or an emotional support dog.

National VA Dog Trainer – a VA employee with extensive canine training and program management experience. This individual was based in Atlanta and was responsible for supervising and coordinating the efforts of the Local VA Dog Trainers.

Pairing - the training process in which a handler was given instruction and practice in commanding and caring for a service dog or an emotional support dog. The pairing process for service dogs took place at the contracted dog vendors' locations; the pairing process for emotional support dogs took place at the handlers' home, facilitated by a VA Dog Trainer.

Paired – indicates that the pairing process was complete.

Participant - a Veteran enrolled in the study after completing informed consent.

Per Protocol (PP) Dataset - the data from the population of participants who were paired with a dog based on their initial randomization assignment, which included data after some participants received a replacement dog for various reasons.

Per Protocol Dog Replacement (PPDR) Dataset – the Per Protocol (PP) data minus any data collected after a replacement dog was received.

Post Visit – refers to an assessment visit for the CAPS, which was largely collected at month 15.

Proofing – the performance evaluation of service dogs or emotional support dogs by the VA National Dog Trainer against the training standards listed in the contract Statement of Work. If tested successfully, VA would accept the dog for the study.

Randomization – a method used for assignment of participants to a treatment group in a study based upon chance.

Service Dog- a dog that is trained to perform one or more tasks to mitigate a disability, as defined by the Department of Justice per the Americans with Disability Act (ADA). There are differences in terminology, and the term "assistance dog" is often used internationally as an alternate to "service dog." In this report the term "service dog" will be used, sometimes abbreviated as "SERV." Service dogs have legal access rights in public spaces, housing, and commercial transport aircraft (see related definition for "emotional support dog").

Study Chair – the individual providing leadership for the study and ensuring that the study is performed in accordance with the protocol.

Study Protocol – the original research plan that includes a complete description of study participants, outcomes, objectives, methodology, statistical plan, and other relevant information. The IRB reviews and approves the study protocol.

VA Chief Veterinary Medical Officer (CVMO) – the senior veterinarian in VA; a member of the Executive Committee who also had primary responsibility for contract management.

VA Veterinarians – Veterinarians employed by VA who were responsible for oversight of all dog-related matters (dog medical record and training standards, dog purchase contracts, dog delivery schedules, and interactions with dog vendors).

Visit – a home or clinic assessment that occurred after dog pairing at weeks 1 and 2, and months 1, 2, 3, 6, 9, 12, 15, and 18 with outcome assessments of participants at month 3 and thereafter.

Abbreviations

AAA- Animal-Assisted Activity
AAI- Animal-Assisted Intervention
AAT – Animal-Assisted Therapy
ACAA – Air Carrier Access Act
ADA – Americans with Disabilities Act
ADI – Assistance Dog International
AE – Adverse Event
AKC – American Kennel Club
APA – American Psychiatric Association
AVMA – American Veterinary Medical Association
CAPS – Clinician Administered PTSD Scale
CDC – Centers for Disease Control and Prevention
CGC – Canine Good Citizen
COR – Contracting Officer's Representative
CPRS – Computerized Patient Record System for the Department of Veterans Affairs
C-SSRS – Columbia Suicide Severity Rating Scale
DAR – Dimensions of Anger Reactions
DOD – Department of Defense
DOJ – Department of Justice
DSM-V - Diagnostic and Statistical Manual of Mental Disorder, fifth edition
EMOT – Emotional Support Dog
FCS – Fully Conditional Specification
HIPAA – Health Insurance Portability and Accountability Act
IACUC – Institutional Animal Care and Use Committee
IGDF - International Guide Dog Foundation
IRB – Institutional Review Board
ITT - Intent to Treat
ITTRS – Interactive Touch Tone Randomization System
LSI – Local Site Investigator
MCS – Mental Component of Veterans Rand 12 (VR12) Item Health Survey
MedDRA - Medical Dictionary for Regulatory Activities
MI – Myocardial Infarct
MINI – Mini International Neuropsychiatric Interview Version 7.0.0
NESARC-III - National Epidemiologic Survey on Alcohol and Related Conditions-III
n (or N) - Number
NMDA - N-Methyl D-Aspartate
PCL-5 – PTSD Civilian Checklist-5
PCS – Physical Component of Veterans Rand 12 (VR12) Item Health Survey
PE- Prolonged Exposure Therapy
PHQ-9 – Patient Health Questionnaire
PP – Per Protocol Dataset
PPDR – Per Protocol Dog Replacement Dataset
PROMIS – Patient Reported Outcome Measure Information System
PSQI - Pittsburgh Sleep Quality Index

PTSD – Posttraumatic Stress Disorder
RCT – Randomized Clinical Trial
RR&D – Rehabilitation Research & Development
SAE – Severe Adverse Event
SBI – Suicidal Behavior or Ideation
SD – Standard Deviation
SERV – Service Dog
SF-36 - Mental Outcomes Study Short Form 36
SOW – Statement of Work
TSA – Transportation Security Authority
VR-12 – Veterans Rand 12 Item Health Survey
Vs - Versus
WHO-DAS 2.0 - World Health Organization Disability Assessment Scale II
WPAI:GHP - Work Productivity and Activity Impairment Questionnaire: General Health Problem

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1. Introduction

A. Review of PTSD

i. Clinical definition and diagnosis

Post traumatic stress disorder (PTSD) falls under the heading of trauma and stressor-related disorders in the Diagnostic and Statistical Manual of Mental Disorder fifth edition, commonly known as DSM-V or DSM-5 (APA, 2013). The criteria require that a person has experienced a significant trauma or a series of traumas with manifestations across four individual symptom clusters: 1) intrusion, 2) avoidance, 3) negative alterations in cognitions and mood, and 4) alterations in arousal and reactivity. Characteristic PTSD symptoms include persistent intrusive memories of the trauma, avoidance of trauma-associated stimuli, cognitive distortions of guilt or blame associated with the trauma, and hyperarousal from innocuous environmental triggers resembling aspects of the trauma (APA, 2013). PTSD often is accompanied by mental health conditions such as personality, mood, anxiety, and nicotine, drug, and alcohol use disorders (Smith, et al., 2016). The resultant impacts are disability, decreased mental health functioning, poor quality of life, and an inability to reintegrate fully into society (Gellis, et al., 2010; Pittman, et al., 2012; Goldberg, et al., 2016).

PTSD emerged as a separate DSM diagnosis in 1980 and is often considered a signature condition among military Veterans. Epidemiological studies of the US population establish the lifetime prevalence of PTSD as 7.8% (Kessler, et al., 1995) with women experiencing PTSD at a rate twice that of men (10.4% versus5.0%); a consistent finding across populations and methods (Tolin & Foa, 2008). Among US military Veterans, prevalence estimates have varied from approximately 12% to 30% (Hoge, et al. 2004, 2008, 2014; Thomas, et al., 2010; Seal, et al., 2007; Kulka, et al.,1990) according to military service during a war era, service branch, deployment status, and combat exposure. In fact, odds ratios of PTSD for deployed versus non-deployed Veterans varied from 1.42 (95% Confidence Intervals (CIs): 1.31, 1.53) for Operation Iraqi Freedom/Operation Enduring Freedom era to 3.58 (CIs: 3.07, 4.17) for Vietnam era (Magruder & Yeager, 2009).

Several advances occurring in the past decade have deepened our understanding of the neurobiology of PTSD and modeling of fear circuitry believed to lie at the core of PTSD pathophysiology. The primary brain centers responsible for extinguishing fear circuitry following specific stimuli (e.g., reminders) lie within complex circuitry between the basolateral amygdala and the medial prefrontal cortex. Individuals who develop PTSD have large fear field areas within the basolateral amygdala, which serve to activate the central nucleus of the amygdala resulting in physiological and behavioral expression of fear. Fear extinction circuits, which counterbalance fear expression, also lie within these centers. When sensory stimuli previously associated with trauma are repeatedly presented in the absence of danger, the fear expression response elaborated by activation of the amygdala is normally extinguished due to inhibitory input from the medial prefrontal cortex, but these inhibitory effects are lessened in PTSD. In effect, PTSD can be understood as a disorder that impedes the switching between fear expression and fear extinction states.

For decades now, clinicians have witnessed improvements in PTSD symptoms upon prescribing antidepressant therapies such as serotonin reuptake inhibitors and mixed class

antidepressants, as well as anti-adrenergic agents like prazosin (VA/DOD PTSD Clinical Practice Guidelines 2017). However, even with first-line antidepressant treatments, response rates are typically less than 60% and remission rates less than 30% (Berger, et al., 2009) indicating the need for continued exploration of novel pharmacologic treatments. Some examples of these investigated treatments include: d-cycloserine, which presumably acts to augment extinction of fear conditioning via its action as a partial agonist at the N-methyl d-aspartate (NMDA) receptor; stellate ganglion blockade, in which anesthetic is injected into sympathetic nerve bundles in the neck in order to theoretically inhibit neural connection between the peripheral sympathetic nervous system and the cerebral cortex in elaborating the 'fight or flight' response; and 3,4-methylenedioxy-methamphetamine, a psychoactive controlled substance, which has been demonstrated to dampen amygdala activity and is being utilized to augment psychotherapy in the treatment of PTSD (Heresco-Levy, et al., 2002, Baker, et al., 2017, Rothbaum, et al., 2014; Lipov & Ritchie, 2015; Mulvaney, et al., 2014; Peterson, et al., 2017; Oehan ,et al., 2013; Mithoefer, et al., 2018. These interventions have often demonstrated robust benefit in non-blinded studies typically lacking placebo controls, but prospective randomized controlled trials have thus far been inconclusive and/or generated mixed results and smaller effect sizes.

Complimentary to the development of neurobiological targets, advances in non-pharmacological interventions for PTSD have progressed. Evidence-based psychotherapies, such as Prolonged Exposure Therapy and Cognitive Processing Therapy, have demonstrated even greater effect size and duration of benefit in the treatment of PTSD, and several leading agencies now recommend psychotherapy treatments over pharmacotherapy (Stein, et al., 2006; Haagen, et al., 2015).

PTSD has a profound impact on quality of life and functional status. The United Nations published data on PTSD worldwide using the metric of disability adjusted life years (DALYs), which can be thought of as one lost year of "healthy" life. (WHO, 2004). This report found the US near the top of all countries, and PTSD "costs" 58 DALYs per 100,000 population -- the same rate as for Parkinson's disease in the US. In part because PTSD remains a heterogenous condition that contains multi-causal factors and is multi-modal, it is often very complex to treat. As such, while the measure of success for PTSD treatments is reduction in specific symptoms, treatments that improve functioning and quality of life are lagging far behind. There is a clear need for treatments that improve functioning and quality of life which can be implemented in concert with existing treatments to shorten the time to improved functional status.

ii. PTSD in Veterans

In 2010, overall prevalence of PTSD in VA primary care clinics was 11.5% (Richardson, et al., 2010). As the number of women Veterans increases (10% of Veteran population in 2018 and estimates of 14% by 2033) (Yano, et al., 2010), it is predicted that higher rates of PTSD will be found in this population, which can be associated with sexual and physical assault (Zinzow, 2007).

The detrimental impact of PTSD is particularly challenging for the Veteran population. The number of Veterans with PTSD within the VA population has increased dramatically in the past years, with nearly 400,000 Veterans diagnosed with PTSD between FY2002 and FY2015 (Group EPP-DH). This increase is largely due to Operation Enduring Freedom and Operation Iraqi Freedom, but also, there are increasing numbers of Veterans from all eras seeking treatment and disability claims, including a recent doubling of PTSD cases among Vietnam-era Veterans seeking VA mental health treatment. In addition to the negative impact of PTSD on quality of life, there are

multiple other mental health comorbidities associated with PTSD, including Major Depressive Disorder, other anxiety disorders, eating disorders, substance use disorders, and suicide, as well as increased risk for dementia and overall mortality (Kessler, 2000; Panagioti, et al., 2009; Harned, et al., 2006; Brewerton, 2007; Nock, et al., 2009; Yaffe, et al., 2010).

One of the biggest challenges of managing PTSD, relative to other commonly encountered mental health conditions, is that treatments tend not to be as effective in all individuals and remission rates remain relatively low at approximately 30-40% (Jonas, et al., 2013; Difede, et al., 2014), and PTSD is projected to remain a chronic and debilitating condition for many Veterans. Therefore, the development of additional therapeutic interventions that will decrease limitations on activity and improve quality of life remains of utmost importance. A promising augmentation strategy is the use of service dogs, one that has successfully decreased limitations and increased quality of life for individuals with a variety of chronic and disabling conditions, including sensory (visual and auditory), and mobility impairments. As a complement to standard evidence-based treatments, the proposed use of service dogs could provide adjunctive treatment to improve functional outcomes in PTSD; however, a systemic review of the literature indicated the published research on effectiveness is limited, and much of the data remain anecdotal.

B. Service Dogs, Emotional Support Dogs, and Other Types of Dogs

i. Overview of the Human-Animal Bond: Dogs as Human Companions

The benefit of human-animal bond for Veterans has a long history in the United States. Animal-assisted therapy dates back to at least 1919 when dogs were part of therapeutic interventions for psychiatric patients (Chumley, 2012). Since then, dogs have assisted physically disabled Veterans, participated in a variety of animal-assisted programs, helped rehabilitate soldiers while training service dogs for others, and provided stress control for deployed combat units (Chumley, 2012). Ritchie and Amaker (2012) reviewed the military's use of dogs in combat and operational stress control units and their potential for easing PTSD symptoms; however, as the authors noted, the review is based on observations and personal accounts.

Dogs are currently the most popular companion animal species in the United States; an estimated 38% of US households own at least one dog (AVMA Pet Ownership and Demographics Sourcebook, 2017-2018 edition).

Although many animal species have served as human companions, dogs and cats predominate. These two species are the ones primarily associated with what has come to be called "the human-animal bond." Nobel laureate Dr. Konrad Lorenz and Dr. Boris Levinson are credited equally with originating the concept of this bond (Hines, 2003). In 1983, Dr. Leo Bustad officially coined the phrase "human-animal bond" (Hines, 2003). Only within the last 20 years has our understanding of this bond evolved from "feel good" explanations to scientific validation.

Lorenz believed that there is a basic psychosocial mechanism responsible for cooperation between humans and animals described through the development of trustworthiness between the two. As mentioned by Sable (2013), "There is now convincing scientific evidence that companion animals have positive effects on psychological and physical well-being, helping shape how people regulate their emotions, deal with stress or trauma, and relate to others" (p. 93). Findings involve a synergistic combination of happenings and theories, one of which is the "biophilia hypothesis" (Beck, 2014; Beetz, 2017; Borgi & Cirulli, 2016). This suggests that humans are innately attracted

to things that are alive. The “attachment theory” is used to describe the emotional relationship between an infant and mother, but the theory has been applied to the human-dog bond as well (Beck, 2014; Borgi & Cirulli, 2016). In both theories, attachment is based on facial signals, like the eye gaze, and on facial features associated with neonates, such as a relatively large head, large eyes, and infant-like appearances.

Recent studies have identified several physiological components to human-dog attachments. The most significant of these is the inverse relationship between the neuropeptide oxytocin, which facilitates affiliative interactions, and the stress hormone cortisol. There is an interspecies, positive-facilitated loop between gazing and increasing oxytocin levels (Beetz, et al., 2012; Kis, et al., 2014; MacLean, et al., 2017; Nagasawa, et al., 2015; Pop, et al., 2014; Romero, et al., 2014). Additionally, this loop works through the hypothalamic-pituitary-adrenal axis to reduce the stress hormone cortisol (Beetz, et al., 2012; Handlin, et al., 2012; Nagasawa, et al., 2015; Pendry & Vandagriff, 2019; Pop, et al., 2014). Studies of dogs can also show corresponding significant increases in β-endorphins, prolactin, phenylacetic acid, and dopamine (Pop, et al., 2014; MacLean, et al., 2017).

Physiological changes correlate with physical and mental benefits of human-dog bond. The landmark study by Friedman, et al. (1980) found that in a population of individuals who had a myocardial infarction, pet owners were significantly more likely to survive the next year compared to survivors without pets. Specifically, they demonstrated the protective effect of pet ownership by exploring the one-year survival of 92 individuals who had suffered myocardial infarcts (MIs). Only three of 53 individuals who owned pets (6%) had died at one-year post MI, compared to 11 out of 39 individuals who did not own pets (28%). All 10 individuals who owned pets other than dogs had survived the year. Although some studies do not support positive health effects (Herzog, 2011; Wells, 2019), there is now a large body of research data connecting positive results with animal ownership, particularly dog ownership. Dog owners tend to have a slower resting heart rate (Allen, et al., 2002; Pop, et al., 2014), lower blood pressure (Allen, et al., 2002; Anderson, et al.,1992; Arhant-Sudhir, et al., 2011; Pop, et al., 2014; Wells, 2019), lower cholesterol levels, (Anderson, et al., 1992; Arhant-Sudhir, et al., 2011), and better triglycerides levels (Anderson, et al., 1992; Arhant-Sudhir, et al., 2011). They also experience longer post-MI survival (Arhant-Sudhir, et al., 2011; Wells, 2019) and better pain management (Carr, et. al., 2018). Simply stroking a dog decreases physiological arousal, as indicated by a reduction in the blood pressure (Lynch, et.al., 1974; Vormbrock & Grossberg, 1988), heart rate (Friedman, et al.,1980), and respiratory rate (Friedman, et al.,1980). Just having a dog present is associated with significantly lower blood pressure readings than when one is not present (Beetz, et al., 2012; Jarolmen & Patel, 2018). There is also a faster recovery of the cardiovascular and immune systems from stressful events (Allen, et al., 2002) to a degree that is significantly better than having a human friend present instead (Campo & Uchino, 2013). Even when adjusted for age and physical activity, people who walk their dog have less diabetes, hypertension, and hypercholesterolemia than those who do not have a dog or who have a dog but do not walk it (Lentino, et al., 2012). According to other studies, individuals with companion animals visit the physician less often (Aiyama, et al., 1986; Headey, 1998; Siegel, 1990), use less medication (Aiyama, et al., 1986; Headey, 1998; McHarg, et al., 1995), and have better overall physical health (Anderson, 1992; Putney, 2013; Siegel, 1990). These health benefits are apparently dose-related. The longer dog ownership occurs, the lower the risk of cardiovascular disease (Xie, et al., 2017).

Dogs can reduce stress and anxiety levels (Putney, 2013) and improve mood (Beetz, et al., 2012; Wells, 2019). Dellinger (2009) reported on the use of dogs for emotional support when traumatized witnesses testified in court. Animal-assisted therapy (AAT) has shown positive results when used with hospitalized children (Tsai et al., 2010), adolescents hospitalized in psychiatric units (Bardill & Hutchinson, 1997), and adults on psychiatric units diagnosed with borderline anxiety (Barker & Dawson, 1998). Additionally, analysis of hospital records indicated that patients who participated in AAT had reduced pain (Ichitani & Cunha, 2016; Stoffel & Braun, 2006), increased relaxation and calmness (Stoffel & Braun, 2006), and better attitudes during the AAT sessions (Stoffel & Braun, 2006). Dogs have been shown to have beneficial effects in the mental health, quality of life, and well-being of wounded warriors (Beck, et al., 2012; Mills & Hall, 2014), nursing home residents (Colombo, et al., 2006; Friedmann, et al., 2015), and institutionalized people such as those in prisons (Wells, 2019). Additionally, the presence of a dog has been correlated to a reduction in depression (Lentino, et al., 2012; Putney, 2013), fear and anxiety (Beetz, et al., 2012; Beetz, 2017; Putney, 2013), and aggression (Beetz, et al., 2012; Beetz, 2017). There is also an increase in trust toward others (Beetz, et al., 2012; Beetz, 2017), calmness (Beetz, 2017), mood (Beetz, et al., 2012; Mills & Hall, 2014), motivation (Beetz, 2017), sense of purpose and self-worth (Kabel, et al., 2015; Mills & Hall, 2014), empathy (Vidović, et al., 1999),and learning (Beetz, et al., 2012).

Peacock, et al. (2012) reported that the human-animal bond can be particularly strong for individuals who are psychologically vulnerable. The physical presence of a dog helps fill the human need for attention and emotional intimacy (Borgi & Cirulli, 2016), and daily care provides a feeling of worth and a distraction from negative events (Mills & Hall, 2014). The stress of living alone, moving frequently, or dealing with social interactions can be reduced by a dog by adding companionship and facilitating social interaction (Bueker, 2013; Faver & Cavazos, 2008; Mills & Hall, 2014; Putney, 2013; Wells, 2019).

According to a study published in 2013 by an international group of scientists (Wang et al., 2013), convergent evolution shaped genes in humans and dogs that correspond to diet, behavior, and disease. Dogs have developed the ability to read a person's behavioral and communicative cues (Hare & Tomasello, 2005).

Dogs have a genetically predetermined willingness to observe human faces and make eye contact (Miklósi, 2003). As a result, both dogs and humans pay attention to others in social interactions using their tactile-kinesthetic, visual, auditory, and communication abilities. Cognition studies show that dogs are able to interpret complex social interaction cues such as cross-pointing, reverse directions, and different arm extensions (Hare & Tomasello, 2005; Miklósi et al., 2003; ; Miklósi & Soproni, 2006; Soproni, et al., 2002). Even when a person is unaware of his or her involuntary movements, the dog is watching the non-verbal signals, considering them a priority—higher than a consciously spoken word or manifested gesture (McConnell, 2003). These same cues, coupled with positive reinforcement, are important in training dogs to certain tasks and ultimately for successful bonding of a person with their service dog or pet. LaFollette, et al. (2019) found the use of positive reinforcement with service dogs resulted in a stronger bond and higher amount of attachment behavior and playfulness than when other training methods were used.

ii. Legal Guidelines for Service Dogs and Emotional Support Dogs

In 1929, The Seeing Eye, Inc was the first program to train dogs for the blind (Sachs-Ericson, et al., 2002). Since that time, additional non-profit organizations and companies have been created which train dogs to help individuals with a variety of disabilities. The manner in which the dog assists individuals varies and is a function of the needs of the individual. Table A provides an overview of the different types of dogs utilized by people with disabilities and the dog's purpose.

Table A. Types of Dogs for People with Disabilities

Type of dog	Purpose
Guide dog	Helps individuals who are blind or have diminished vision with navigation.
Hearing dog	Alerts individuals with hearing impairments to different sounds, such as phone ringing, doorbell, approaching traffic.
Medical alert service dog	Signals the onset of a medical event (such as a seizure or changing blood glucose level in an individual with diabetes), stays with individual during a medical event, may go for help or call 911.
Mobility service dog	Retrieves objects, braces during transfers, pulls wheelchairs, acts as stabilizer.
Mental health service dog	Tasks vary depending on organizational preferences and handler needs but may include reminding the handler to take medicine, providing safety checks or room searches, interrupting self-mutilation, and removing disoriented individuals from dangerous situations. All service dogs in the study were trained as mental health service dogs.
Emotional support dog	Provides emotional support for people with disabilities, such as anxiety or depression. Unlike the dog types listed above, these dogs are not trained to do specific tasks to mitigate a disability, and do not have public access rights to accompany their handler into places where pet dogs are not normally permitted. Emotional support dogs are not considered service dogs per the ADA.
Therapy dog	Added to this table for the sake of completeness and clarity, these dogs are brought into a variety of healthcare and educational facilities by their owners for the benefit of people who interact with them during the visit as part of AAT. They are not service dogs and are distinct from emotional support dogs in providing a benefit to others versus the handler. They have no special legal access privileges beyond what pets have. Several organizations have certification programs for these dogs to ensure that the dogs are not aggressive and are tolerant of affection from strangers.

A service dog is trained to do work or perform tasks for people with disabilities**.** The work or task a dog has been trained to provide must be directly related to the person's disability (ADA, 2010). Examples of such work or tasks provided by the Department of Justice include guiding people who are blind, alerting people who are deaf, pulling a wheelchair, reminding a person with mental illness to take prescribed medications, and calming a person with PTSD during an anxiety attack (ADA, 2010). Service dogs are working animals, not pets, and are protected under the Americans with Disabilities Act (ADA). Aside from special circumstances where the presence of the service dog "fundamentally alters" the nature of services (for examples, a sterile operating

room), the ADA states that a service dog is entitled to accompany their disabled handler into public buildings. Only two questions can be asked of a handler with a service dog (ADA, 2010):

- Is the dog a service animal required because of a disability?
- What work or tasks has the dog been trained to perform?

Staff members are not allowed to request any documentation for the dog, require that the dog demonstrate its task, or inquire about the nature of the person's disability. Only if the animal is misbehaving (i.e., dog is out of control and cannot be brought under control by handler or is not housebroken) can the management of that business request the dog and handler to leave (ADA, 2010).

In contrast, emotional support dogs can be characterized as pets but they do have some legal accommodations beyond those provided to pets, as will be discussed. The term itself, emotional support animal, is a Department of Justice term for a pet that provides therapeutic benefit to its owner with a disability through companionship and affection. Though not specifically trained to perform tasks to help with a person's disability, emotional support dogs are expected to be well behaved (including being housetrained) and to not pose a danger to other animals or people. Dogs whose sole function is to provide comfort or emotional support do not qualify as service dogs under the ADA and thus do not legally have access to public buildings.

Though not covered by the ADA, emotional support dogs are given special protections under the US Department of Justice, Civil Rights Division (DRC, 2011). In the U.S., the Fair Housing Act and the Air Carrier Access Act of 1986 are two federal laws that grant special privileges to owners of emotional support animals. The Fair Housing Act has a provision which allows individuals with disabilities to live in housing with their emotional support animal without being charged any additional rent that might normally be applied because of a pet. The Air Carrier Access Act (ACAA) provides a process in which a person with a disability may travel with his/her animal, as long as it has been prescribed and the owner has appropriate documentation (DRC, 2011). It should be noted that this is a rapidly developing area, and the U.S. Department of Transportation is in an ongoing rulemaking process to potentially discontinue the boarding rights granted emotional support dogs and other species, due in part to increasing in air incidents of aggression and unsanitary incidents caused by poorly trained emotional support animals. Table B provides summary information on the two types of dogs (DRC, 2011).

There is some potential confusion between a service dog "task" learned by the dog to reduce handler anxiety and the comfort provided by the presence of an emotional support dog. In an example provided by the Department of Justice, if a dog is trained to sense that an anxiety attack is about to happen and takes a specific action (task) to help avoid the attack or lessen its impact, that would qualify as a service dog. However, if the dog's mere presence provides comfort, that is not be considered a task and the dog is not considered to be a service dog (US Department of Justice, 2015; Q4).

Table B. Federal Accommodations for Service and Emotional Support Dogs

Dog allowed in:	Service Dog	Emotional Support Dog
Housing	Yes per Americans with Disabilities Act (ADA)	Yes per Fair Housing Act. Documentation of disability may be needed.
Place of Employment	Yes per ADA	No
Public Space	Yes per ADA	No
Commercial Aircraft Cabin	Yes per ADA	Yes, but pending changes in Air Carrier Access Act may bar future access. Documentation of need from a mental health provider required.

C. Animal-Assisted Therapy (AAT)

AAT can be considered a subset of activities under the larger umbrella of animal-assisted activities, which refers to the use of the human-animal bond to benefit people. In the specific context of mental health conditions, AAT involves the use of animals, such as horses, dogs, cats, and others as a therapeutic intervention meant to complement traditional therapy (Psychology Today, 2020). Examples of AAT utilizing dogs are a therapist bringing a dog to a health facility to interact with patients, and having Veterans interact and train dogs for use by others (Beetz, 2019). Although the use of service dogs might be considered to be an AAT activity, it is important to note that service dogs are not "therapy dogs" (see Table A). Kamioka, et al.'s (2014) systematic review of animal-assisted therapies using randomized trials identified only 11 trials, with low study rigor. Outcomes examined in the trials found were symptomatic in nature. Similarly, O'Haire, et al.'s (2015) systematic review of animal-assisted Interventions (AAI, a term sometimes used interchangeably with AAT) for use with individuals who had psychiatric conditions provided findings on 10 studies. All but one of these studies were done at a location other than the person's home, and all were small sample sizes. Outcomes were a decrease in symptoms, including depression, PTSD and anxiety.

Focusing on service dogs, there has been limited research completed to examine the impact of service dogs have on their human counterparts. Table C provides a brief summary of research on service dogs mitigation of mobility and PTSD mental health impairments. Allen & Blascovich (1996) conducted a randomized, controlled clinical trial of 48 individuals who were wheelchair dependent; participants either received a trained service dog one month into the study or were wait-listed to receive a service dog after 13 months. The positive effects observed in participants included improved self-esteem, social integration, and independence (Allen & Blascovich, 1996). Study designs have included descriptive survey as well as the use of pre-post designs (Rintala, 2002; Collins, 2006), trying to capture aspects of the participant's life prior to receipt of the dog and compare it after receipt or pairing. A few randomized trials exist for mobility impairments. Mental health service dog studies have been primarily focused on symptom reduction.

Table C. Brief Summary of Service Dog Research

Author	Type of Impairment Possibly Mitigated by the Service Dog	Sample Size (N)	Study Design	Outcomes
Allen & Blascovich, 1996	Mobility	48	Randomized Clinical Trial	Mobility dogs improved participation, work outcomes and social interactions
Collins, et al., 2006	Mobility	152	Cross-sectional/ four groups	No difference in functional outcomes between groups
Fitzgerald, 2006	Mobility	123	18-month follow up	Those on the waiting list had poorer functional outcomes
Lloyd, et al., 2019	Mental Health	199	Descriptive, survey	Service dogs provide varying help to people with mental health diagnoses
O'Haire & Rodriquez, 2018	PTSD	141	Non-randomized, efficacy trial	PTSD patients paired with service dogs had a decrease in symptoms compared to those not paired with service dogs
Rintala, et al., 2002	Mobility	22	Pre-post-test/no control	Increase in social interactions
Vincent, et al., 2017	PTSD	15	Cross-over design	Service dogs showed short term benefits to their owners.
Yarborough, et. al., 2017	PTSD	78	Descriptive	Service dogs helped subjects in preventing panic, and putting space between themselves and others

Winkle, et al.'s (2012) literature review of the use of service dogs for individuals with mobility disorders cited 371 papers that discussed the topic. Of those, only 12 met a higher level of evidence using the American Academy of Cerebral Palsy and Developmental Medicine 5 level evaluation system (Darrah, et al, 2008). Of those 12 papers, only one randomized clinical trial (RCT) exists (Allen, et al., 1996); this study reported that trained service dogs significantly helped people who used wheelchairs to live independently. Unfortunately, there has been much debate about the study, and several researchers (Eames and Eames, 1996; Rowan, 1996) have criticized it. Concerns included an inability to determine the source or training status of the dogs in the study, the lack of attrition, and the high rate of study participants returning to work (82%) – surprising given the high rate of unemployment of individuals with severe disabilities (CDC, 2008).

The goal of rehabilitation is to aid those with disabilities and chronic conditions to return successfully to the fullest possible life at home and the community. Sayer, et al. (2010) reports that 49% of Veterans returning from OEF/OIF have problems participating in community type activities. For other disabilities, dogs have proven to be instrumental in helping those individuals regain independence and live successfully in the community. Collins, et al. (2006) presented

cross-sectional findings using data from a large prospective study (Fitzgerald, 2006) to ascertain the impact on psychosocial well-being and community participation across four groups – people recently paired with a service dog, people on a wait list to receive a service dog, those with a pet and those with no pet. Collins' (2004) results found no significant differences across groups with respect to community participation. Fitzgerald's (2006) study, which was a longitudinal assessment of the same group of participants, indicated that those subjects on the waiting list to receive a dog had a greater decrease in social interaction than the other three groups (paired with service dog, owns a pet, no dog).

Eddy, et al. (2008) observed the public's behavior toward individuals using wheelchairs with and without their service dogs. When an individual had his/her service dog, an increased number of strangers smiled and initiated conversations compared to when the dog was not present. These results were noted first with children and then with adults in a variety of settings (Eddy, et al., 2008). Fairman & Huebner (2000) also reported that those with service dogs were more likely to engage in society, and they were approached more in public. Hart et al. (1987) reported more community participation as measured by shopping trips and more approaches that were social in nature. Others have reported similar findings with respect to social interaction and participation in leisure activities (Lane et al., 1998; Rintala et al., 2002).

Some research has indicated that community participation can increase at least partly because an individual feels safer with a service dog. (Sachs-Ericsson et al., 2002). Serpell (1991) showed that the population in general feels safer with the presence of a dog. Studies conducted by Fairman & Huebner (2000), Hart et al., (1987), and Valentine et al., (1993) all reported that those with service dogs reported feeling safer or more willing to go out at night by themselves.

Quality of life has also been examined. Shintani's (2010) study included 38 subjects, 10 of whom had mobility service dogs. The study utilized the Mental Outcomes Study Short Form 36 (SF-36), a self-reported general assessment of quality of life as it relates to an individual's health (McHorney, et al., 1993). Significantly higher scores (indicating higher quality of life) were seen in the Physical Functioning and Role Emotional subscales of the SF-36. The Mental Component Summary score was also significantly higher in those who had the service dogs. Other studies have shown improved quality of life when an individual has a mobility service dog (Rintala et al., 2002). O'Haire's and Rodriquez's research (2018) compared Veterans with and without a mental health service dog trained to mitigate PTSD symptoms. Results showed improvement in the PTSD Checklist-5 (PCL-5) over time as well as improvements in quality of life and social functioning.

Loneliness has been correlated with a higher likelihood of anxiety, fatigue, and depression (Katcher, 1985). Pet ownership alone was found to reduce loneliness by facilitating social interaction and providing constant companionship according to several researchers (Vombrock & Grossberg, 1988; Lynch, et al., 1974; Todd-Schuelke, et al., 1991), but not by others (Collins, et al., 2006; Fitzgerald, 2006). Valentine, et al., (1993) reported participants with mobility or hearing impairment that had service dogs felt less lonely, less depressed, more capable, and more confident. Likewise, Mowry et al., 1994 found the presence of hearing dogs was associated with recipients feeling more relaxed, improved physical well-being, and safer as compared to the absence of a hearing dog. Some participants in an interview-based study of 26 abused women reported that their pets were the reason they did not commit suicide (Fitzgerald A, 2007). To our knowledge, no randomized trial has been performed regarding the impact of any dog type on suicidality.

As previously mentioned, except for the 2018 O'Haire and Rodriguez study, little published research exists on the benefits of service dogs as a treatment for PTSD. Much of what has been described is limited to anecdotal reports published online and in lay journals. These reports include dogs helping individuals with panic disorders (Fields-Meyer, 2006), bipolar disorder (Smith et al., 2003), symptoms of PTSD including overcoming flashbacks, reduction of nightmares, anxiety, as well as medication use (Kime, 2012; McLaughlin, 2012; Ruiz, 2012; News 10, 2013). One study (Esnayra and Love, 2008) sampled 71 individuals who self-reported information on their demographics, mental health care and diagnosis, and information regarding using a service dog for help. All but six participants were either partnered with a service dog or were in the process of receiving one. The authors acknowledged that the sample was convenience based, and drawn from individuals who were members of a mental health service dog listserv. Based on self-report, in this cross-sectional study, 84% of the study population stated their symptoms decreased as a result of having the dog (Esnayra and Love, 2008).

Herzog, 2011 has reported that much evidence in the literature reporting the beneficial effect of pets on human well-being suffers from a number of serious procedural and interpretation flaws, and negative results are often overlooked or weighted less than positive reports. For example, Parker et al., 2010 reported that pet owners were more likely than non-pet owners to die or be readmitted to the hospital within a year of experiencing a heart attack. And elderly adults who claimed to be highly attached to their dogs were found to be more depressed than their counterparts who were less attached to pets (Miltiades and Sherer, 2011). Furthermore, for some people, dog ownership is a source of stress due to daily care responsibilities, the financial burden of food, grooming and veterinary care for the dog, and the overall time commitment that dogs require (Fallon, 2017). Similarly, stress over poor behavior, additional burden of care of a living being, and trauma / grief surrounding injury or death of the animal due to the shorter lifespan of dogs as compared to humans. These pragmatic concerns also apply to service dogs and emotional support dogs. Service dogs, particularly if wearing a "service dog" vest, may cause unwanted and even negative attention for the owner (Rory, 2018).

There have been no randomized clinical trials completed that examined the potential benefits of service dogs for Veterans with PTSD. As shown in the literature presented in this background section, service dogs can mitigate other types of disabilities, such as spinal cord injury and hearing problems. In addition, some mental health outcomes have improved with the introduction of a service dog. Given this, further research was needed to assess the impact of service dogs on quality of life and function for individuals with mental health challenges, such as PTSD.

D. Legislative Mandate

The significant number of anecdotal reports on the benefit of service dogs for Veterans with PTSD led to a public and legislative push for VA to provide Veterans with veterinary insurance for mental health service dogs, in addition to service dogs for visual, hearing, and mobility impairment, for which this benefit was already provided. Therefore, the design of this study was in part determined by Section 1077 of Fiscal Year 2010 National Defense Authorization Act that required the VA to "conduct a scientifically valid research study of the costs and benefits associated with the use of service dogs for the treatment or rehabilitation of Veterans with physical or mental injuries or disabilities." Elsewhere in the Bill it was specified that "or mental injuries or

disabilities'" include posttraumatic stress disorder. The Bill required that matters studied should include assessment of the therapeutic and economic benefits of using service dogs, quality of life benefits, savings on health care costs regarding hospitalization, use of prescription drugs, and gains in productivity and employment. The scientific data from this randomized controlled trial, rather than relying on anecdotes, are expected to guide future VA benefits policy for use of service dogs for Veterans with mental health diagnoses, most commonly, PTSD. The mental health outcomes will be reported in this monograph, followed by the health economic assessment and findings in a second monograph.

E. Phase I Study

i. Overview of Study

In 2011, investigators at the James A. Haley Veterans Hospital received VA Rehabilitation Research & Development (RR&D) Service funding (Award # D8094I) to conduct a three-year non-randomized longitudinal study, known as the Phase 1 study. The Phase 1 study began in July 2011 and was designed to compare two groups: 1) participants receiving usual care for PTSD; and (2) participants receiving usual care and a mental health service dog. The intent was to determine whether provision of a service dog intervention improved the mental health of Veterans with PTSD. These outcome measures included change in PTSD symptoms, community participation, and health care utilization. Study participants completed standardized instruments to assess mental, physical, and psychosocial health as well as healthcare utilization before and after receiving a mental health service dog. Three service dog organizations (vendors) were engaged contractually to provide mental health service dogs for the study.

Despite efforts to recruit participants into the usual care only arm, only one Veteran was recruited. Several significant adverse events related to poor dog health and training occurred, and recruitment was suspended in August of 2012. The principal adverse events were (i) dog bites experienced by children of two study participants, (ii) multiple service dogs with clinically significant hip dysplasia, and (iii) the death of a service dog, likely due to an undisclosed but diagnosed coagulation disorder. Although not a factor in suspending the study, one service dog was euthanized due to an incurable neurologic neoplasm.

At study suspension 60 participants had been enrolled; of those, 24 had been paired with a service dogs and 44 of the enrolled participants were dropped from the study for various reasons. Nine participants paired with service dogs were withdrawn. Of those nine, one participant's service dog died, four participants returned the service dog to the vendor, and four service dogs remained with their participant. Fifteen participants kept their service dog and completed the study. Because of the small number of participants completing the study and the skewed participant responses related to the many dog-related difficulties, a priori analyses were not possible. However, a tremendous amount of information and experience was gained, leading to multiple key improvements in the current study.

ii. Lessons learned

Caring for living animals requires significant investments in energy and time, and many challenges exist with animal-based interventions relative to a medication or device. Key lessons

learned from the Phase 1 study that were applied to the current (Phase 2) study are outlined below:

- Comparison/control group: In the Phase 1 study, only one person agreed to participate when assigned to a usual care only group. Despite its importance in making the study conclusions more generalizable, the research team determined it was not feasible to include a usual care control group in the Phase 2 study. Before reaching that conclusion, the team weighed the challenging problems of not focusing on the opportunity to receive a dog in study recruitment materials, with the potential benefit of reducing the dropout rate for the usual care group. In weighing these challenges, the study team determined that it could be unethical to recruit participants with no expressed interest in receiving a dog as this requires investment (commitment to caring for a dog) as well as study design challenges (high dog return rate and/or a high dropout rate in the dog groups). Also, it is unethical to ask participants to stop utilizing their existing PTSD therapies to allow a comparison of a dog only group (utilizing an unproven potential mitigation for PTSD) versus a dog plus usual care group (severely compromising the principle of individual medical care for the advancement of generalizable knowledge). Therefore, it was decided that the best option was for each person to be their own control by comparing data before and after receiving the dog intervention.

- Addition of the emotional support dog group: As has been discussed in the Introduction, there is ample evidence that the bond between a dog and a human provides benefits to people. The question of interest here, however, is whether the benefits from a service dog (public access, ability to complete specific PTSD-related tasks) extend beyond the general benefits of the human-dog bond? To this end, it was decided to compare outcomes for a provision of a service dog versus an emotional support dog, which neither performs trained tasks nor has the ADA public access rights of a service dog. While it could be of interest to disentangle the relative benefits of public access from PTSD-specific tasks, current ADA regulations prohibit one without the other.

- Information captured: Throughout the course of the Phase 1 study, participants noted repeatedly that the standardized measures used to monitor symptom status and community participation did not adequately cover what the service dogs were really doing to help them. Therefore, these Phase 1 participant observations resulted the addition of an open-ended interview at the end of the study.

- Dog quality: Based upon discussions with Phase 1 participants, it became clear that once a Veteran receives and bonds with a dog, they are reluctant to give up the dog even when it is unhealthy or is a bite risk for the family. These Phase 1 observations informed the current design by not placing the burden of ill dog health or poor dog training solely upon the Veteran to identify or disclose. To this end many changes were made when obtaining and training dogs for the study (see Table E for details). When a Veteran is concerned with their dog's training or health, PTSD can distort this emotional burden (e.g., guilt, hypervigilance) and further exacerbate PSTD symptoms overall. For example, there were Veterans in the Phase 1 study whose dogs barked at other dogs and became very anxious in venues such as sports events, leading to those Veterans being even less likely to venture out in public because of the embarrassment of poor dog behavior. Accordingly,

those organizations that seek to serve Veterans (and often use a Veteran focus in fundraising) have a deep obligation to make sure they provide the best possible mental health service dogs. In addition, the ability of handlers with mental health diagnoses to navigate the challenges of a poorly trained dog in the team's experience can be greatly diminished in comparison to handlers who struggle with mobility disorders. No community guidelines specific to training and pairing mental health service dogs with handlers who have PTSD were available until 2017 when Assistance Dogs International published a set of guidelines for use by its member organizations (four years after planning for the current study was completed and three years after recruitment started). Table E lists the specific changes made to the current study protocol based upon this consideration of obtaining the best possible dogs for the study and ensuring that any adverse events with the dogs were communicated promptly to the study team.

- Dog deaths. During the Phase 1 study, two service dogs died. One service dog died most likely due to a clotting disorder not disclosed to VA. The Veteran in that case was upset but did not request a replacement dog and dropped out of the study. A second service dog died from a neurological tumor, which adversely affected the Veteran participant's PTSD symptoms. VA provided a replacement, which resulted in resolution of the PTSD exacerbation. These examples illustrated the need for the study team to quickly and effectively address dog health conditions to mitigate the impact of unforeseen events on Veterans' PTSD and study participation. Within service dog organizations, handlers who have experienced the death of a service dog are usually given priority consideration in receiving a replacement service dog to minimize the impact of the dog's death on the handler, if the handler is ready for another dog. VA followed the same practice. In the current study, one dog was hit and killed by a motor vehicle and a second dog was presumed to be dead after apparently being hit by a motor vehicle (see 3. Methods – *i. Withdrawals*).

- Knowledge of dogs and dog care: In the Phase 1 study, it was apparent that the knowledge of dogs and experience with dog ownership varied greatly across individual participants. Because the ability to properly care for a dog, knowing when to seek veterinary medical care, and understanding the overall expense associated with dog ownership are crucial to the health and well-being of the dog, the participants in the current study were required to take a dog care online course and then complete a set of course assessment questions before receiving a dog. Observations of Phase 1 participants who had a good grasp of dog care lead to the team's belief that dog care knowledge would not only improve the care of their dog but also would help reduce the dropout rate. The full course content and assessment questions are available on the online: (https://www.research.va.gov/programs/animal_research/PTSDstudy.cfm).

- Generalizability of the study outcomes and incidence of dog bites: The team was very cognizant of the need for the service dog results to be generalizable to the larger service dog provider community, and VA had no special expertise in that area, so vendors were not provided with a prescribed dog training protocol. This performance-based approach relied very heavily on a thorough proofing process done personally by VA's National Dog Trainer, which reduced the incidence of biting dogs from 2 (children) of 24 (8.3%) in the Phase 1

study (estimated Dunbar scale [Dunbar] 2 bites, dog's teeth did not puncture the skin) to 2 (adults) of 181 (0.55%) in the current study (both Dunbar scale 2 incidents), a fifteen-fold reduction in incidence.

In summary, although the Phase 1 study was initiated, successfully recruited Veterans with PTSD, and ultimately paired them with mental health service dogs, a number of problems occurred related to vendor practices that were beyond the control of the study team. The decision was made to stop recruitment and use the lessons learned to inform the current study. Subsequently, the current research study (See Table D) was designed with additional safety measures implemented to protect both the participants and study dogs (both service dogs [SERVs] and emotional support dogs [EMOTs]).

Table D. Phase 1 study design features, adverse events encountered, and resulting improvements in study design *

Problematic Phase 1 Study Design Feature	Phase 1 Study Adverse Events	Current Study Approach
Vendors selected the dogs trained as SERVs without study team member oversight. Vendors used rescue dogs with uncertain behavioral and health histories.	Approximately 25% of the SERVs developed clinical signs of hip dysplasia within 15 months of pairing; health problems identified by veterinarians during health screening were not shared with VA.	Detailed health screening requirements were added to the dog procurement contract, using Department of Defense (DoD) working dog standards as the basis; however, some medical requirements of the VA contract exceeded those of the DOD. Medical records had to be provided to VA veterinarians for review and approval before dog was included in the study. Only purpose-bred dogs were used.
Vendors screened dogs for aggression and decided when each was fully trained and ready to be paired with a participant without study team member oversight.	Children of two study participants were bitten by the study dogs (possibly rescue dogs), and it was discovered that many dogs were poorly trained.	Detailed training standards were added to the procurement contract. The American Kennel Club (AKC) Canine Good Citizen (CGC) test was used as the standard for good behavior for all study dogs; in addition, the Assistance Dogs International (ADI) Public Access Test and AKC Community Canine Test were used to evaluate the performance of SERVs and EMOTs, respectively. The VA National Dog Trainer proofed all dogs against contract standards prior to purchase.
Vendors conducted post-pairing training with participants without study team member oversight.	Vendor staff discouraged participants from reporting problems to VA, and inflated expectations, thus biasing study outcomes.	VA dog trainers (not vendor staff) interacted with participants post-pairing to ensure problems were identified quickly and biasing statements were minimized.

*A full copy of the contract statement of work incorporating the process improvements above in dog health and training requirements for vendors is available on the online: (https://www.research.va.gov/programs/animal_research/PTSDstudy.cfm).

F. Current Study Aims

The major aims of this study were as follows:

1. The primary aim was to determine whether overall disability and quality of life of participants with PTSD was improved by the provision of SERVs relative to the provision of EMOTs. The special tasks (see rationale for task selection below) that the SERVs were trained to perform were expected to benefit participants with PTSD and thereby, provide more improvement than the emotional support dogs, which provided comfort and companionship only.

2. The secondary aim was to compare the impact of SERVs versus EMOTs on mental health outcomes. Participants who received trained SERVs were expected to have reduced PTSD symptoms, decreased suicidality, depression, and anger, as well as, improved sleep outcomes in comparison to participants who received EMOTS that provided only comfort and companionship.

SERV tasks were selected by a team of mental health professional with expertise in PTSD with input from service dog organizations and Veterans suffering from PTSD. The task descriptions below are consistent with those outlined by Saunders, et al., 2017.

- Lights: The SERV finds and turns on a light switch in a darken room. This task was requested by Veterans, particularly women Veterans in the Phase 1 study, who had experienced military sexual trauma.

- Sweep: The SERV enters a room and sweeps the perimeter to detect an intruder. This task was specifically requested by women Veterans in the Phase 1 study, who had experienced military sexual trauma.

- Bring: The SERV retrieves an object specified by the handler. Service dog organizations reported this is the most common SERV task regardless of the service dog's specific purpose because recipients find it helpful in their daily lives. The bring task may have a role in promoting more interaction of the handler with their environment by the dog bringing items of interest, such as newspaper or phone or in some cases, potentially therapeutic items (e.g. walking shoes, cane, or medications). Similarly, the bring task enhances the independence of handlers with other physical disabilities or injuries who have difficulty bending over, or who use adaptive equipment such as a wheelchair, by enabling the dog to deliver dropped items to them.

- Block: The SERV stands in front of the handler to provide a barrier between the handler and the approaching person. The task ensures the handler's personal space is maintained by the dog in a non-aggressive manner.

- Behind: The SERV stands behind the handler to provide a barrier between the handler and the person approaching from behind. The task also ensures the handler's personal space is maintained by the dog in a non-aggressive manner.

To this end a longitudinal, randomized, intent-to-treat, two-arm, parallel design, multicenter clinical trial was conducted at three VA medical centers: Atlanta VA Healthcare System (Decatur, GA; Site 508), Iowa City VA Healthcare System (Iowa City, IA; Site 584) and the VA Portland Healthcare System (Portland, OR; Site 648).

2. Contract Requirements

A. Background

The National Defense Authorization Act of 2010 required VA to partner with nonprofit 501(c)(3) organizations that were accredited by or adhered to the standards of Assistance Dogs International (ADI), an accrediting organization with demonstrated experience, national scope, and recognized leadership and expertise in the training of service dogs and education in the use of service dogs. After conducting an extensive review of proposals and conducting site visits to candidate organizations, VA awarded contracts to three vendors on 7/8/14. Based on past performance and VA site visits, the three organizations that were awarded contracts had the professional staff, resources, and canine training experience to deliver high quality well-trained dogs in sufficient number within the time frame of the study. One vendor was a well-recognized and longstanding service dog provider accredited by ADI; this vendor maintained a large canine breeding colony. The other two awardee organizations were experienced military working dog vendors and procured dogs from external sources. Prior to beginning work on the contract, all contractor employees and subcontractor employees requiring access to VA information and VA information systems completed cyber security and VA Privacy training.

For details not provided in this section, the entire text of the contract statement of work is available on the web: https://www.research.va.gov/programs/animal_research/PTSDstudy.cfm.

B. General Requirements

All dogs eligible for purchase by VA were evaluated on their ability to meet the standards set forth in the contract statement of work (SOW). The SOW stipulated that candidate dogs be one of the following breeds: Labrador Retriever, Golden Retriever, Labrador Retriever-Golden Retriever cross, or German Shepherd. These dog breeds were preferred because of their trainability and tractable personalities. The SOW allowed other breeds to be considered if they met the specified contract requirements and were approved by the contracting team through the VA Contracting Officer. Dogs of either gender were acceptable as long as they met the age, size and weight requirements stipulated in the SOW. The medical, temperament, and physical requirements for SERVs and EMOTs were identical; all three vendors provided both types of dogs. Because the dogs that bit children in the Phase 1 study were from shelters or had uncertain histories, only purpose-bred canines with known medical and behavioral histories were acceptable for the study.

In addition to acceptable performance during testing, all candidate dogs were required to be extremely tolerant of people (regardless of age, race or disability), be generally attentive and friendly toward people, display good socialization, and be free of anxiety around people and other animals. All three vendors were required to submit technical proposals as part of the contracting process. The technical proposals detailed how candidates would be trained as either an emotional support dog or a service dog.

A stepwise process was used. The behavioral profile of emotional support dogs and service dogs was similar (see previously listed characteristics); both required the same high arousal threshold for perceiving social stress because of the potential intensity of interactions with Veterans with PTSD. Candidate dogs displaying certain behaviors such as equipment sensitivity or anxiety in crowded situations precluded them from placement as a service dog, but not as an emotional support dog since these dogs do not accompany their handler in public spaces. These characteristics were the basis for candidate dog selection.

All candidate dogs were exposed to a wide variety of environments, people, and situations to ensure they were well-socialized and did not show stress reactions to learning. The candidate dogs entered a professional training program focused initially on basic obedience, temperament evaluation, and behavioral assessment. Dogs were evaluated for a wide variety of traits including but not limited to aggression, anxiety, handler focus, comfort wearing equipment, confidence, sociability, and reactivity to novel stimuli. Through an iterative evaluation process, some dogs were deemed inappropriate for participation in the study based on behavior or temperament. These dogs were either placed in a different type of working role or adopted to a private home as a pet. Candidate dogs that persistently demonstrated behavior or temperament traits that would create a management or safety concern when performing task work or when working in public (e.g. being easily distracted by small animals, anxiety around revolving doors or crowds, discomfort wearing a service dog vest, etc.) but were otherwise interactive with their handler, low management, and of sound temperament were designated as emotional support dogs. Emotional support dogs live in a home and community environments where all dogs are readily accepted (i.e. dog parks); therefore, distractibility and novel environment sensitivity is of less concern because they do not have public access rights. For these dogs, training concluded once they were successfully able to meet the standards of the American Kennel Club Canine Good Citizen and Community Canine tests. Finally, the dogs that demonstrated the ability to maintain focus, behave appropriately and perform in a wide variety of environments continued to progress in the service dog program and were trained in the specific tasks chosen for the study and to meet the standards of the Assistance Dogs International Public Access Test.

C. Medical Requirements

For all dogs that met the general requirements, the vendor provided documentation of health and soundness of dogs being considered for purchase. Each dog was identified with a unique implanted microchip number. Documentation of dog health and soundness was provided in the form of an electronic medical file that included radiographs of elbows and hips, vaccination records, health history, veterinary visits for illness, comprehensive physical examination including laboratory testing of blood, urine, and feces, and other required medically related documentation (e.g. administration of preventative internal and external parasite treatments).

The VA SOW required candidate dogs to a hip grade of “good” or better at 14 or more months of age, based on the Orthopedic Foundation for Animals scoring system (for military working dogs, a hip grade of fair is usually acceptable). After the contracts were awarded, VA also agreed to accept a Penn-HIP index value of <0.30 taken at 16 weeks of age or older, as recommended by the University of Pennsylvania (http://www.aaha.org/blog/NewStat/post/2010/11/15/925638/Study-compares-PennHIP-OFA.aspx). A dog’s elbows also had to be free of radiologic evidence of degenerative joint disease.

D. Medical File and Training Record evaluation

Electronic medical files for each SERV or EMOT to be considered for purchase by the VA were evaluated by one or more VA veterinarians in the office of the Chief Veterinary Medical Officer, who also functioned as the contracting team subject matter experts (the “Contracting Officer’s Representatives” , or “CORs”), responsible for ensuring that contract performance was monitored and there was good communication between the VA and the vendor staff. In some cases, additional medical testing and/or treatment was requested to ensure a dog was healthy. Some dogs were rejected because of conditions that could impact their working life, such as potentially progressive ophthalmic or cardiac anomalies. Dogs that were judged to be sound and in good health were medically cleared by VA veterinarians and written notification of medical clearance was provided to the vendor. From the pool of medically cleared dogs, vendors selected trained dogs that were ready for proofing (performance testing against the contract training standards) by VA. The training records of candidate dogs were electronically provided to the VA trainer and the CORs at least one week prior to the scheduled proofing date. Training records contained detailed documentation of temperament and behavioral evaluations, socialization to people (particularly children), other animals, and a variety of environments (i.e. home and public settings) as well as documentation of training hours and proficiency in the applicable performance standards.

E. Dog Performance Standards and Testing

The vendors provided VA a list of medically-cleared EMOTS and SERVs (identified by name and microchip number) that have been trained and had passed the applicable performance tests when conducted by vendor personnel. Vendors were required to provide documentation of training and training competency. American Kennel Club (AKC) Canine Good Citizen (CGC) certification is a long standing and well-recognized program that is used to assess good behavior and obedience in dogs. The AKC CGC was required for both dog types to ensure dogs were well-behaved and had mastered basic obedience training. The AKC CGC test consists of 10 test items (see below); the dog is expected to be well-behaved and not display shyness or resentment.

1) Demonstrates the dog is receptive of an unfamiliar person approaching and interacting the handler.

2) Demonstrates the dog is receptive of being petting by the unfamiliar person in item 1.

3) Demonstrates the dog is receptive of undergoing physical examination or grooming.

4) Demonstrates the handler’s ability to control the dog while out for a walk including turns and stops.

5) Demonstrates that handler and the dog can move successfully negotiate pedestrian traffic.

6) Demonstrates the dog responds to the commands site and down and stays in place.

7) Demonstrates the dog will come when called by the handler from a distance of 10 feet.

8) Demonstrates the dog is well-behaved when encountering another handler and their dog.

9) Demonstrations that the dog can remain calm and not become obviously startled by distractions.

10) Demonstrates the dog remains calm and well-behaved with another handler when briefly separated from the owner or primary handler.

To pass, a dog must successfully complete all ten items during a single testing session.

The EMOTs were further evaluated using the AKC Community Canine test, the most advanced level of the CGC program to test the dog's obedience training in natural (community) settings. Some aspects of the Community Canine test are similar to the CGC but they are evaluated under more challenging conditions. All ten items must also be successfully completed in one session and are described below:

1) The dogs stands, sits, or lies down and waits while the owner/handler is occupied with a task or interacts with another person in a setting such as a park.

2) The dog walks on a loose leash with the handler at a fast and slow pace as well as makes a left turn, right turn, and stop in a community setting.

3) The dog walks on a loose leash in crowded community setting such as festival or fair.

4) The dogs walks past other dogs and handlers in a community setting and does not pull at the leash.

5) The dog sits and stays in a group setting of three other dogs with their handlers.

6) The dog accepting petting from a person carrying a bag of some type; the bag is placed on the ground before petting the dog.

7) The dogs ignores food on the ground or in a dish when the handler directs the dog to "leave it."

8) The dog is on a 20 ft line in a down or sit position and stays while the handler walks away to pick up an item and then returns to the dog.

9) The dog comes when called by the handler who is 20 feet away despite the present of distractions.

10) The dog stays in a sitting or standing position while the goes through a doorway and then comes when called by the handler.

The skilled tasks performed by SERVs were intended to help mitigate their handler's disability. SERV were required to respond to AKC CGC, the five skilled tasks, and the ADI Public Access Test (PAT) commands when given by the handler 90% of the time on the first ask in all public and home environments. The five skill tasks are described below:

Block (stand in front of Veteran to give space). Trainers will be asked to demonstrate the ability to have the dog provide physical space in front of the handler. The dog should perform the task reliably each time and should not have to be given a command more than three times before complying.

a. This task shall be demonstrated in a public place. The handler will walk with the dog for at least 30 feet distance then and stop. The dog should naturally stop with the handler. As a person approaches from the front the block command will be given. The dog should step in front of the handler, typically the dog stands perpendicular to the handler, to provide a physical barrier between the handler and the person approaching.

b. The dog should be relaxed and not exhibit aggressive, defensive, or protective behaviors. The dog should not show interest in the person approaching and should stay in block position until released by the handler with an appropriate command.

Lights (locates and turns on lights) Trainers will be asked to demonstrate the ability of the dog to enter a room ahead of the handler and turn on the lights to ensure good visibility, reduce the risk of falls, and generally make the Veteran feel more at ease. This is a task that will be performed in the subject's home and should be demonstrated in a home or simulated home environment. A standard consumer light switch must be used (touch plates or similar adaptive hardware are not acceptable).

a. To demonstrate the skill, the handler will walk the dog to a door or entryway and give the command to turn on lights. The dog should enter the room and turn on a light while the handler remains in the entryway.

b. Once the lights are on, the dog will return to the handler's side and wait for further direction.

Sweep (room, perimeter, turn on lights, if needed). Trainers will be asked to demonstrate the ability of the dog to enter a room ahead of the handler, turn on lights, and sweep the perimeter of the room. The dog should perform this task reliably each time and should not have to be given a command more than 3 times before complying. The dog must bark if an intruder is detected. This is a task that will be performed in the subject's home and should be demonstrated in a home or simulated home environment.

a. To demonstrate the skill, the handler will walk the dog to a door or entryway. If it is necessary to turn on lights (meaning a light switch is not accessible to the handler from the door or entryway) a command will be given.

b. The dog should enter the room and turn on a light while the handler remains in the entryway. A command will then be given for the dog to do a sweep of the room.

c. Once it is established that the room is clear, the dog will return to the handler's side.

d. If the dog detects someone in the room it will alert the handler by barking.

Bring (retrieves an object at the request of the handler). Trainers will be asked to demonstrate the ability of the dog to bring specified items to the handler upon request. The dog should perform the task reliably each time and should not have to be given a command more than three times before responding. This task may be applicable to both the home and public environments.

a. To demonstrate the skill, the handler points to a specific object and gives the command.

b. If the specified object is in a group of objects, the handler will say the name of the object in combination with the handler pointing to the object.

c. Once the dog correctly locates the specified object, the dog carries the object to the handler and releases the object to the handler.

Behind (stand behind Veteran to give space). Trainers will be asked to demonstrate the ability to have the dog provide physical space behind the handler. The dog should perform the task reliably each time and should not have to be given a command more than 3 times before complying.

a. This task should be demonstrated in a public place. The handler will walk with the dog for at least 30 feet then stop. The dog should naturally stop with the handler. The dog will be given the watch command and should step behind the handler to provide a physical barrier behind the handler. The dog should stay in "behind" position until released by the handler. Next, the handler should take the dog to a check-out counter or other place where they would need to stand in a line or stand in a group or crowd of people. The dog will be given the behind command and should step behind the handler.

b. The dog should not exhibit aggressive, protective, or defensive behaviors.

c. The dog should be alert but not show interest in or seek attention from the people behind the handler.

d. The dog should stay in the behind position until released by the handler.

The Public Access Test (PAT) commands were given verbally and include controlled unload out of a vehicle, approaching a building (dog stops when handler stops), controlled entry through a doorway (dogs waits for handler to enter), heeling through a building (dog is near handler and unobtrusive), six foot recall on lead, sits on command, downs on command, noise distraction (no fear or aggression), restaurant (proper behavior and unobtrusive), off lead control, and controlled load into vehicle. The dog must be responsive to and successfully complete all PAT

commands. The purpose of the PAT is to ensure the safety of the dog and the handler. SERVs must be under the control of the handler at all times and must be consistently well-behaved and unobtrusive in public settings. A detailed description of the PAT is available at: https://www.research.va.gov/programs/animal_research/ptsdstudy.cfm.

Disqualifying behaviors for the AKC CGC, AKC Community Canine, and ADI PAT were the same, with dogs being disqualified for any indication of aggressive behavior, such as growling, baring teeth, raising hackles, etc. or eliminating during testing. Defects in behavior displayed at any point during evaluation or participant assignment were cause for rejection.

Proofing was conducted at the vendor's location by the VA National Dog Trainer. The vendor provided all necessary materials and equipment for proofing. Because dogs are more at ease when working in familiar surroundings with a known trainer, the VA National Dog Trainer purposely conducted proofing in novel public settings for added rigor in testing. Each candidate dog was tracked with its unique implanted microchip number. Only dogs that successfully passed proofing were paired as SERVs or EMOTs with participants. Additional training was required for dogs that failed initial proofing; in general, any dog that failed proofing twice was eliminated from further consideration. The disposition of dogs that did not meet VA contract standards was determined by the vendor. Some dogs were re-purposed as another type of working dog and others were adopted into private homes. Medically cleared and proofed dog that did not initially match with a participant may have subsequently matched with another study participant.

F. Vendor requirements

The vendors were required to make travel and accommodation arrangements for participants who received a SERV; pairing occurred on the vendor's property. VA reimbursed reasonable transportation, travel, and per diem costs for the participant in accordance with the Federal Travel Regulations – Federal Acquisition Regulations 31.205.46, "Travel Costs."

EMOTs were shipped to the participant's study site. Vendor and local site study personnel coordinated the shipping arrangements; these costs were reimbursed by VA. VA dog trainers confirmed that the dog's signalment (i.e. age, sex, and breed), weight, coat color and implanted microchip matched the billing of lading information.

G. SERV pairing

Participants randomized to the SERV group traveled to the vendor's location for training to become a qualified handler. The vendor made travel arrangements for the participant and arranged reimbursable accommodations and food during the training session. Typically, training for SERV pairing was one week at all vendor sites but for participants who required additional training, it was extended up to two weeks. The pairing process covered basic obedience commands, execution of the specific trained tasks, basic dog care, and the public access rights given SERV by the ADA. Vendors provided a certificate of participant/SERV pairing and a written summary of the pairing procedure (referenced by the dog's name and microchip number) to the COR. Vendors also provided to the participant a card summarizing the public access rights of service dogs established by the ADA.

H. EMOT pairing

The VA local dog trainer worked with participants to schedule delivery of the EMOT to the participant's home or a suitable nearby locale. The local dog trainer instructed the participant on how to handle his/her dog, which typically occurred over the course of a single day. A second day was scheduled as needed. Once the participant was competent in handling his/her dog, the dog trainer provided the following to the participant:

- Important contact information.
- A photo identification for the EMOT and a brief summary of the dog's right under US law on the back of the card.
- If applicable, a letter signed by the LSI establishing the right of an EMOT to live in housing where pets are not allowed.
- If applicable, a letter signed by the LSI establishing the right of an EMOT to fly in the cabin with the participant for commercial air travel.
- A reminder that EMOTs do not have public access rights and that participants should not try to pass off their EMOT as a SERV (such as by using a service dog vest).

I. VA Dog Trainer Support

The potential influence of the vendor on the participant was minimized after SERV and EMOT pairing for the duration of the research study by having Veterans rely on the VA dog trainers for assistance once they had received their dog. Dog trainers hired by VA were responsible for monitoring the bonding of the participant with their study dog and had primary responsibility for interacting with the participants after pairing. Nonetheless, VA dog trainers were encouraged to seek guidance and consult with the vendor as needed should any problems in a pairing arise.

A qualification for participating in the study was identifying a person to be responsible for the dog in the participant's absence (see: 3. Methods C. Study selection criteria). These substitute caregivers (i.e. spouses, partners, and friends) commonly were present when Veteran participants were paired with their SERV or EMOT. In the event, a substitute caregiver was not present for pairing; the local site VA dog trainers assisted the substitute caregivers to ensure they were trained in basic dog care.

J. VA Veterinary Insurance Program

Per §1077(c)(5)(A) of the 2010 National Defense Authorization Act for Fiscal Year 2010, VA provided veterinary treatment to maintain the health of the dog and keep it functioning in its prescribed role throughout the time the Veterans were participating in the study. All SERVs and EMOTs used in the study were provided by and owned by VA. VA partnered with a commercial veterinary insurance company through a contract to provide a unique and comprehensive benefits package for study participants.

Only medically cleared and successfully proofed dogs were approved by VA for veterinary insurance coverage. A requirement of the contract was that all veterinarians who were reimbursed for services rendered to VA owned study dogs under the contract must be properly licensed in their respective states. The insurance coverage included a comprehensive wellness plan and sick/injured insurance coverage.

Unlike commercial veterinary insurance plans, participants were not billed for premiums, deductibles or copayments associated with wellness or sick/injured coverage. With few exceptions there were no “out-of-pocket” expenses to the participants. The comprehensive VA veterinary insurance program for study SERVs and EMOTs provided coverage regardless of age, breed, geographic location or pre-existing condition; no commercially available policy provided this level of coverage.

3. Methods

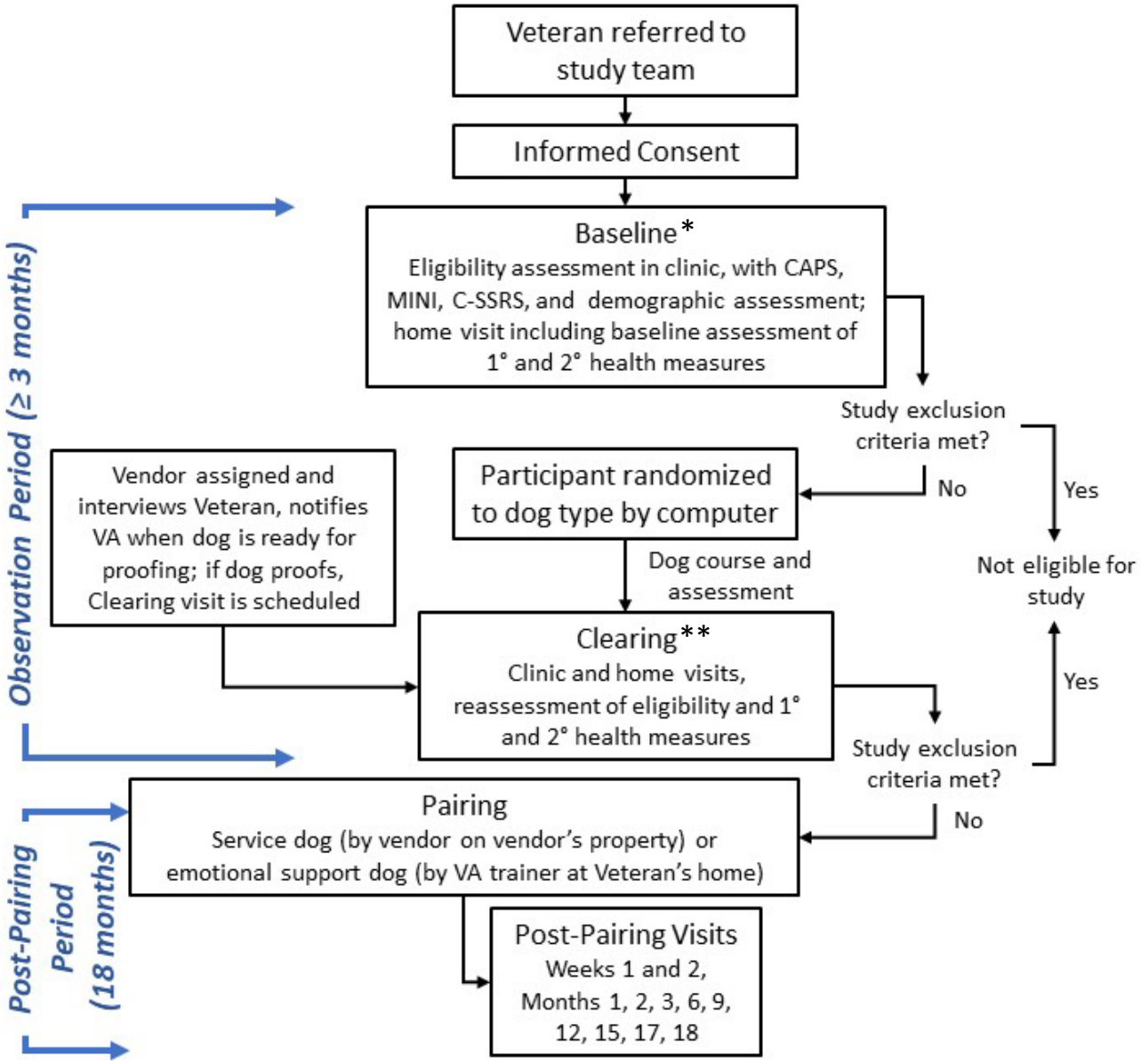
A. Study Synopsis

The basic rationale and design of the trial have been published previously (Saunders et al. 2017) but are summarized below.

From December 2014 through June 2017, participants from the three study sites were recruited. All necessary approvals were obtained including: VA Central Institutional Review Board (IRB, protocol #13-54) for the human subjects protections elements; Institutional Animal Care and Use Committees (IACUCs) at Atlanta (protocol #V001-14) and Iowa City (protocol #1490201) for the animal welfare oversight. IACUC review of the study was considered to be unnecessary by the Portland VA IACUC because the use of dogs in this study did not constitute animal research and therefore, did not technically require IACUC review. Monitoring of the study was provided by a Data Monitoring Committee, which met periodically over the course of the study. The registration number for the study on ClinalTrials.gov was NCT02039843 and was posted on 1/20/14.

Per the study protocol, participants were consented, enrolled, and screened before random assignment to the SERV or EMOT groups. In order to detect a 15% difference in mean scores for MCS (outcome requiring largest sample) over 18 months of follow-up, at a statistical significance level of 0.05 (two-tailed test) and a power of 85%, 82 participants per treatment group was required, and 110 participants per group (220 total) required to account for a maximum of 25% post-pairing participant lost or dropout rate (Saunders, et al., 2017). Thus, the initial goal was to pair 110 participants with a SERV trained in specific tasks related to PTSD and 110 with an EMOT to provide comfort and companionship. After randomization to group, an observation period of at least three months duration began; during this period both the study team and the participants were blinded to the type of dog to which the participant had been randomized. The dog type assignment was revealed to the participant and the study team once the observation period was completed. Subsequently, participants were paired with either a SERV or an EMOT per assignment and followed over an 18-month period, during which they were assessed at multiple time points via a combination of clinic and home visits using a variety of primary, secondary and tertiary outcome measures. Figures E and F respectively, show the basic study flow and the assessment schedule.

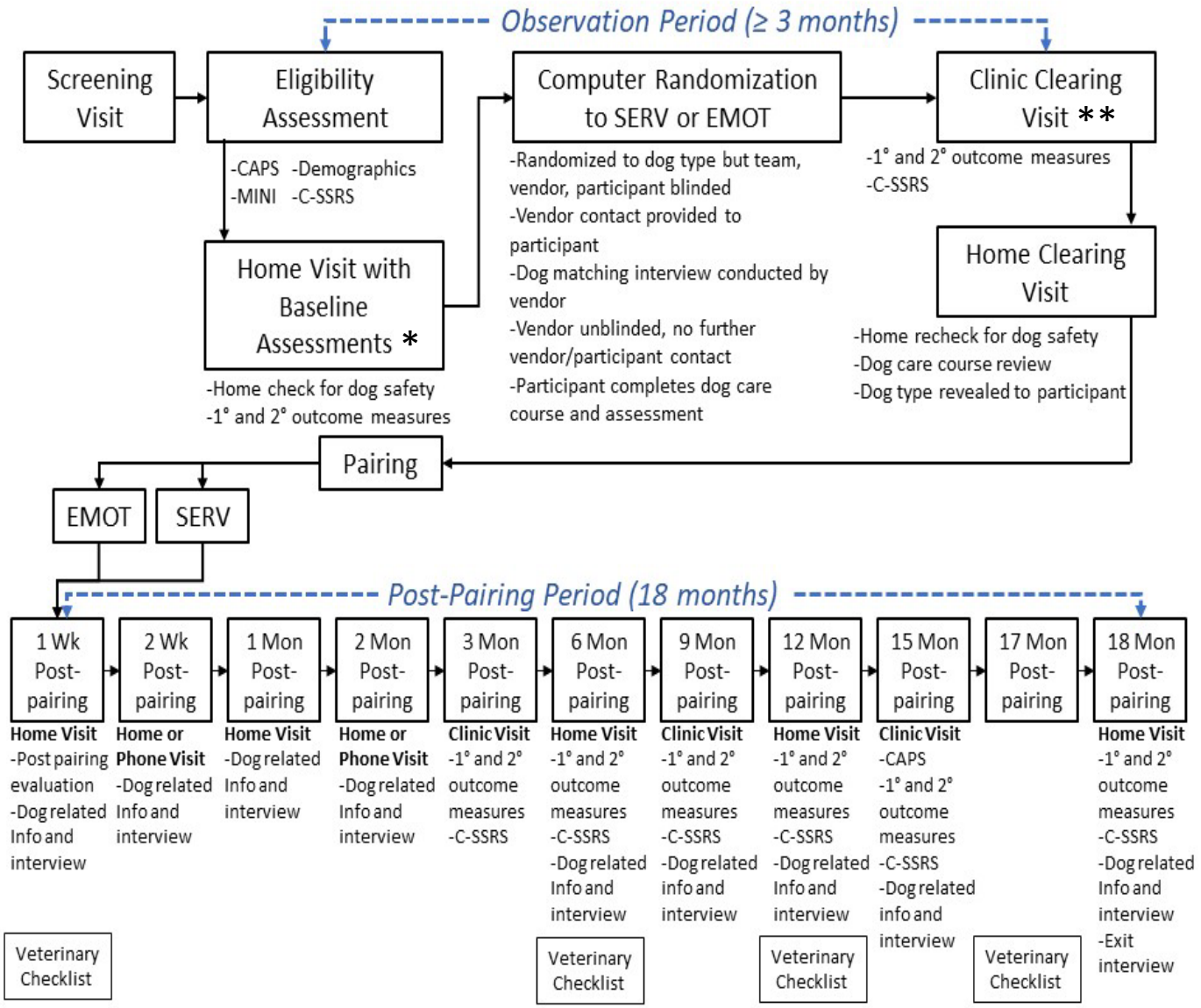
FIGURE E. Study Flow (based upon Saunders, et al., 2017)



* Also referred to as "Baseline 1 testing occurring during home visit" in Saunders et al., 2017.

** Also referred to as "Baseline 2 assessments" in Saunders et al., 2017

Figure F. Study design including mental health measures (based upon Saunders, et al., 2017)



* Also referred to as "Baseline 1 testing occurring during home visit" in Saunders et al., 2017.

** Also referred to as "Baseline 2 assessments" in Saunders et al., 2017

B. Design Considerations

Conducting well-controlled studies involving animals and humans is complex because of the many sources of animal-human interaction bias and the difficulty of controlling handler competence and animal behavior in different environments across study participants. While there are studies that allude to the positive consequences of pet ownership on various psychological and social well-being parameters (Raina, et al., 1999; McConnell, et al., 2011; O'Haire, 2010), the benefits of animal-assisted therapy for specific conditions are not well established. Published studies are of relatively low quality and have many flaws (Stern & Chur-Hansen, 2013; Kamioka,

et al., 2014; Herzog, 2014). Although the study by O'Haire and Rodriguez (2018) reported that the addition of a service dog to usual care was associated with an improvement in PTSD symptoms, this study had at least two significant limitations - participants were not randomized to the treatment group and all participants received a service dog. Studies involving animals and humans are often plagued by the lack of, or inability to incorporate several critical elements to enable valid conclusions including non-treatment groups, controls for novel experiences with animals, written documentation of treatment procedures, blind observations, long-term follow-up. Additionally, studies with animals and humans are often underpowered, rely on self-reports, place a 'positive spin' on negative results, and selectively report data. Specifically, Stern & Chur-Hansen (2013) and Kamioka, et al. (2014) made recommendations for designing future studies, including careful consideration for the selection of study animals and study designs that contain multiple data collection sites and time points. Additionally, it was recommended that authors provide detailed descriptions of the methodology and the intervention, record reasons participants withdrew, describe all adverse events, and specify the cost of the intervention. This study was designed to address all of these considerations, except for the presence of a non-treatment group, for reasons explained in Phase 1 Study description (section 1.E).

The use of dogs as an intervention brings additional complexity because of the need to maintain safety of the dogs, the need to maintain the safety of the human participants and their families, and the fact that the human-dog interaction will change both the dog and the human over the course of the study. Recognition of these issues influenced the study design and the addition of an EMOT group (also described in section 1.E).

A wide variety of study forms were developed to conduct and monitor the study. These forms are summarized in Appendix A - Table YY and are available on the web at https://www.research.va.gov/programs/animal_research/PTSDstudy.cfm.

i. Human and animal safety

The safety of the human participants in the study was enhanced by carefully vetting all dog suppliers (referred to as 'vendors') before the award of contracts to ensure that healthy and well-trained dogs would be provided to participants in the study. Special emphasis was placed on safeguarding children living in or visiting participants in their homes. Once the determination was made to allow children in the home as approved by the IRB (see 3.C. Study selection criteria*),* the following measures were taken if there was a child in the home that was less than 10 years of age:

a. The dog trainer made home visits to the participant at weeks 1 and 2, and at months 1 and 2 to assess whether the dog was comfortable in the presence of the child.

b. The family was provided with educational materials to review with their child/children using components of the American Veterinarian Medical Association (AVMA) Dog Bite Prevention Articles, as well as, being encouraged to read additional materials posted on the website.

c. The participant and family members were instructed to monitor the dog's behavior regarding the dog-child interactions. In particular they were instructed to look out for indicators that the dog was stressed by the presence of the child, such as:

(1) Dog actively avoids the child by hiding, moving away, etc. when the child approaches.

(2) Dog yawns or licks lips when in the child's presence.

(3) Dog snaps or stares at the child.

(4) Dog holds tail higher than horizontal when in child's presence.

(5) Dog attempts to herd child away from the participant or other family members.

(6) Dog displays other behaviors towards the child (or others) that concern the participant.

If the participant or family members observed the behaviors noted above, they were required to immediately contact the local dog trainer or a local study team member. On the initial report of concerning dog behavior, the dog trainer visited the participant's home to evaluate the situation. If, in the dog trainer's judgment, the dog was not comfortable in the presence of the child, the dog was removed from the home and a determination was made regarding the participant's enrollment status.

The safety of each dog was optimized by including very strict study inclusion/exclusion criteria (see 3.C. Study selection criteria). The home of each participant was inspected prior to study enrollment and at regular intervals during the study; veterinary insurance was provided for each dog; there were four mandatory veterinarian visits during the intervention period, and participants were thoroughly trained to handle and care for their dog.

For the combined safety of both the human participant and dog, the bond between the human and the dog was monitored throughout the study, and if issues arose, a member of the study team was available for enquiries and home-visit interventions as needed.

ii. Implications of the human-dog interaction on outcomes

It was essential that participants bonded well with their dogs, and that the bonding endured throughout the study. It was also important that participants took responsibility for ensuring their dog maintained the behaviors that it had been trained to perform. To achieve these goals, the following processes were implemented: (1) through a series of in-depth phone interviews, vendors carefully matched each participant to a dog that had a temperament and physical attributes that would fit with the participant's lifestyle and activity level, (2) the dog-participant bond was monitored throughout the study by the local VA dog trainers, (3) in situations when dog-participant bond was inadequate, a replacement dog was provided if the dog trainers believed this would lead to a stronger bond, and (4) VA dog trainers provided assistance in retraining a dog's behavior and participants' dog handling skills, as needed.

iii. Selection of a comparison intervention

From lessons learned in the Phase 1 study, it was determined in comprehensive discussions among members of the Executive Committee that conducting a three-arm comparator study with a usual care arm and two dog intervention arms would be untenable. A priori, the team determined after review of the literature that a superiority design comparing the SERV intervention with the EMOT intervention was justifiable based on the lack of RCT data comparing the two types of dog interventions in PTSD, and the lack of rigor evident in the SERV dog studies for PTSD. The EMOT intervention was selected as the control as it would allow the researcher to determine if the additional SERV tasks would be superior to PTSD functional outcomes beyond the science portending the physiological benefit of dog ownership, more broadly, as laid out in the introduction (Raina, et al., 1999; McConnell, et al., 2011). In addition, having a control group (EMOT) with no ADA-defined public access privileges would also allow for analyses on this differential benefit afforded to SERV intervention.

iv. Study Personnel

Successful performance of this clinical trial across three VA sites required multiple teams:

- Central Leadership team (Study Chair, Coordinating Center team, Executive Committee, VA Chief Veterinary Medical Officer)- was responsible for study oversight and for making protocol-related and dog-related decisions and for managing and analyzing data.

- Local Site Study Team (local site investigator (LSI; team lead), study coordinator, research assistant(s), and two dog trainers)- was responsible for local data collection. The three LSIs (one per site) served on the Executive Committee.

- Veterinary Team (VA Veterinarians)- was responsible for oversight of dog-related matters (dog medical record review, training standards, dog purchase contracts, dog delivery schedules, and interactions with dog vendors).

- VA Dog Trainer Team (National and local dog trainers)- was responsible for proofing all dogs against contract standards before VA acceptance (National), and for providing consistent support for dog obedience or training problems to study participants (local).

An operations manual was prepared by CSP and distributed to all sites; this manual provided procedural guidance to the study staff.

C. Study Selection Criteria

Veterans were eligible to participate in the study if they lived near one of the three VA sites, if they had received treatment for PTSD in the previous 90 days, and if they were referred by their mental health provider. These prerequisites were used because we wanted to assess the effect of the interventions as adjuncts to, not replacement for, standard VA mental health care for PTSD. Inclusion and exclusion criteria for selection of participants are shown in Table G.

These criteria were selected to maximize participant and dog safety, and to increase the likelihood that a participant would complete the study.

Table G. Inclusion/Exclusion Criteria

Inclusion criteria
1. Males and females - 18 years of age or older.
2. Referral from Mental Health provider that documents PTSD diagnosis.
3. PTSD as a result of any trauma as determined by meeting DSM-V diagnostic criteria.
4. Enrolled in mental health services at VA and has attended at least one mental health visit in the 90 days prior to consent > If individual not currently enrolled in mental health treatment decides to enroll in such then he/she may become eligible to participate in the study. > If individual enrolled in mental health treatment schedules and attends a mental health visit then he/she may become eligible to participate in the study
5. Agrees to remain in mental health treatment throughout the duration of the study.
6. Can adequately care for and handle the dog. > Adequately caring for a dog requires that participants will be responsible for and able to provide food, water, protection, shelter, exercise, transportation, and treatment related to their assigned dog. > Adequately handling the dog means having the ability to give and reinforce obedience commands and control the dog using a leash.
7. Home environment is suitable for a dog. > If the home environment can be remedied the individual may become eligible to participate in the study. > If a participant moves home while enrolled in the study the new home must be suitable for a dog.
8. Home environment is structurally and geographically accessible to study staff. > If the home is geographically inaccessible to study staff and, the individual cannot remedy the situation unless he/she moves home. The study team will not encourage this. If a move takes place, it will be the individual's responsibility to re-contact the study team. > If the individual changes home residence while enrolled in the study, the new home must be geographically accessible to study staff. If it is inaccessible, the dog will be removed and the individual will be withdrawn from the study.
9) Is willing to accept randomization outcome.
10) Has someone to care for the dog during extended absence of the participant. > If no one is available to care for the dog but the situation changes then the participant may become eligible to participate.
11) Others in home are agreeable to having dog. > If others in the home are not agreeable but at a later date the situation changes, then the potential participant may become eligible to participate
12) Is willing and able to travel (by air or car) to the dog vendor training site for pairing if assigned to receive a service dog. > If individual's unwillingness to travel to a training site changes, he/she may become eligible to participate. In this instance, it will be the individual's responsibility to re-contact the study team.
13) Individual has no pet in the home to threaten the bonding and obedience training of an assigned study dog. > If a household dog lives inside the home and the home is partitioned such that there are two or more separate living spaces served by independent entrance/exits, and the

individual does not live in a partition with a dog, then the individual can be eligible. If a household dog lives primarily outside the home in a rural area and the individual is not primarily responsible for feeding the dog on a daily basis, then the individual can be eligible. > If an individual has pets other than dogs that could interfere with bonding, the individual will be scheduled for the screening visits and the relationship will be assessed by the dog trainer. > If an individual has a household dog or other pet that prevents participation in the study but the situation changes, the individual may become eligible to participate. In this instance, it will be the individual's responsibility to recontact the study team
14) Individual can verbalize understanding of consent form, is willing to provide written informed consent and to follow study procedures.
Exclusion criteria
1) Hospitalization for mental health reasons in the past 6 months
2) Aggressive behavior that would make it unsafe for the dog
3) Diagnosis of psychosis, delusions, dementia, moderate or severe alcohol/substance disorder (SUD), or moderate to severe traumatic brain injury as determined by the presence or absence of a condition following scoring of MINI responses or as documented in chart notes. SUD assessment (alcohol/non-alcohol): > Ineligibility is based on the presence of a Moderate (4-5 symptoms) to Severe (6+ symptoms) SUD as identified by the MINI within the previous 12-month period starting from date of the study MINI screening. > If a Moderate to Severe SUD has been documented or communicated by the referring clinician or potential participant or is noted in the EMR prior to the initial MINI screening visit, individuals should be scheduled for their initial screening visit on a timeline commensurate with meeting the 12-month SUDs eligibility window. > If an individual is identified as ineligible during the initial screening visit (i.e. MINI SUDs score ≥4) he/she may be re-evaluated later at the discretion of the study team. Re-evaluations should be scheduled based on a timeline commensurate with meeting the 12-month SUDs eligibility window (absence of a Moderate to Severe SUD for the previous 12 months). If at re-evaluation the individual has <4 symptoms, he/she may become eligible to participate in the study
4) Active suicidal intent as determined by a CPRS flag for suicidal intent or an endorsement of yes to question 5 (active suicidal ideation with specific plan and intent) on the C-SSRS completed at the Clinic Qualifying Visit. > An endorsement of yes to question 4 (Active Suicidal Ideation with Some Intent to Act, without Specific Plan) without endorsement of question 5 indicates that the individual needs additional assessment to determine eligibility.
5) Homicidal intent or cognitive disabilities that would preclude safety of dog and/or ability to participate in the study.
6) Social, mental or physical condition that prevents the individual from either giving informed consent or participating in the study.
7) Participation in another unapproved research trial. > If the individual is in another unrelated study and both the study Chair/PI of this and the other study consider participation in both studies to be acceptable then the individual may become eligible to participate in this study. > If the study Chair/PI of this and/or the other study consider participation in both studies to be unacceptable then, once participation in the other study is complete, the participant may become eligible to participate in this study. At that time, it will be the individual's responsibility to re-contact the study team.

8) Has CPRS flag for violent/disruptive behavior.
9) Potential participants who are pregnant/who have a partner who is pregnant, or who currently have one or more children younger than age 5 in the household for more than 8 hours per day, one day a week will be excluded from the study. > If a participant or anyone else in the household becomes pregnant during the observation period, the participant will be excluded from the study. > Participants who have children in their home/become pregnant after being paired with a dog will be evaluated on a case-by-case basis (see Safety Monitoring of Children in the Home below) > After a total of 10 dogs have been placed with participants who have children between the ages of 5 and 10 years, and after each pairing has successfully reached and passed the 2-month home visit, this exclusion criterion will be revisited for potential inclusion of participants with children younger than 5 years.

Note: Exclusion criteria 1, 3, 4 and 8 were included to increase the likelihood that participants could care for a dog over the study duration; exclusion criteria 2, 5 and 6 were included to maximize dog safety; exclusion criterion 9 was included to maximize participant/family safety, and exclusion criteria 7 and 10 were included to maintain integrity of the research design.

VA's Central IRB (cIRB) approved the project application protocol on 11/15/13. Due to the uniqueness of the study, the protocol was amended multiple times to address issues as they arose. On 4/17/14, the protocol was first amended to include a modification to the study diagram to specify the period of time between randomization and pairing. On 6/2/15, a protocol amendment was approved to revise the exclusion criteria to better reflect DSM V terminology and criteria. An amendment to remove the CAPS assessment measure from the Baseline 2 visit was approved on 7/13/15 to lessen the overall burden on participants by removing the requirement to readminister the CAPS. On 5/23/16, the interval that participants could remain in the observation phase was amended from three to six months to three months to more than one year. The lengthening of the observation phase was a result of participant recruitment exceeding the supply of trained dogs accepted by VA.

At the initiation of the study, for safety reasons based upon previous risks identified in the Phase 1 study, a Veteran could be disqualified from participation because the Veteran/partner was pregnant or currently had children younger than age 10 in the household for more than 8 hours per day, one day a week. Further, if a participant or anyone else in the household became pregnant during the observation period, the participant was excluded from the study. After 20 dogs from each vendor had been placed without an aggression incident involving people, this exclusion criterion was revisited. On 12/16/16, the cIRB approved a protocol amendment allowing participants with children in the home between 5 and 10 years of age to be eligible for enrollment in the study. Participants who had children in their home or became pregnant after being paired with a dog were evaluated on a case-by-case basis. The 12/16/16 amendment also included an extension of the study duration from three years to up to five years due to extended recruitment phase. Lastly, the 12/16/16 amendment approved the CAPS to be administered at the 15 month VA clinic visits instead of the 18 month home visit. Completing the CAPS at the VA clinic would provide immediate access to mental health services should safety concerns be reported by the participant. The protocol was amended on 8/16/17 to add a new procedure to the 18 month visit for assessing dog training retention at the end of the study participation.

D. Outcome Measures

The selection of the primary and secondary outcome measures was challenging for the following reasons: (1) evidence for the mechanism(s) by which SERVs potentially could improve PTSD was lacking, (2) it was challenging to interpret results in a way that would be biologically plausible, and (3) power calculations would problematic due to the inability to specify the effect size for symptom change (Saunders et al., 2017). The research team designed the study so that outcomes would be assessed in terms of impacts on overall mental, social and psychosocial function. Primary consideration was given to the importance of reintegrating Veterans with PTSD into society and effectiveness of a dog in facilitating this process.

i. Primary outcome measures

The two primary outcome measures selected were the World Health Organization Disability Assessment Scale II (WHO-DAS 2.0) and the Veterans Rand 12 Item Health Survey (VR-12), which are described below. A discussion of how the minimal clinically important difference (MCID) was determined for the primary outcomes is presented in Section F. Data Analysis.

WHO-DAS 2.0. The WHO-DAS 2.0 was used to assess health and activity limitations, hereafter referred to as disability. It is a 36-item questionnaire that assesses functioning in six domains during the prior 30 days:

- Cognition: understanding and communicating with the world;
- Mobility: moving and getting around;
- Self-care: attending to one's hygiene, dressing, eating and staying alone;
- Interpersonal interactions: getting along with people;
- Life activities: domestic responsibilities, leisure, and work, and
- Participation in society: joining in community activities.

For each item the participant rates the difficulty they have conducting a task. They respond on a 5-item scale: 'None,' 'Mild,' 'Moderate,' 'Severe' or 'Extreme/cannot do.' Domain scores and a total disability score are obtained. Per the WHO-DAS 2.0 manual, if no more than 2 items are missing overall and no more than 1 item is missing within any domain, the average of the other items in the domain is used for the missing item in that domain to calculate the summary and domain scores. If more than two items are missing overall or any of the domain scores are missing (i.e. when 2 or more items within a domain are missing), then the WHO-DAS summary score cannot be calculated. Also, per the WHO-DAS 2.0 manual, item-response-theory (IRT) based scoring is used to differentially weight items and levels of severity, and to generate standardized domain and summary scores that enable comparisons across populations. Scores can range from 0 to 100 where 0 = no disability; 100 = full disability, thus lower scores indicate better functioning. The WHO-DAS 2.0 was self-administered in paper and pen format at baseline, clearing, and during post-pairing follow-up visits at 3, 6, 9, 12, 15, and 18 months. The timeframe for the WHO-DAS 2.0 was the past 30 days.

VR-12. The VR-12 was used to assess health-related quality of life. It is a 12-item self-administered health survey that assesses health-related quality of life (VR-12; Selim et al., 2009). The VR-12 is a modification of the VR-36, a generic health status measure that has been shown to be valid and reliable in a wide variety of healthcare settings (Ware, et al.,1992; Kazis, 1998). It

yields two subscores: a Physical Component Score (PCS) and a Mental Component Score (MCS). The PCS score reflects general health, physical functioning and role playing and bodily pain. The MCS reflects emotional, vitality/mental health and social functioning. In this study, the survey question regarding problems with work or other regular daily activities as a result of any *emotional problems* (Question 4b) was modified to mirror that of problems with work or other regular daily activities as a result of any *physical problems* (Question 3b). That is, participants were asked the amount they accomplished as they relate to physical (3a) and emotional problems (4a), as well as if they were limited in the kind of work or other activity. Scoring is based on weights derived from the VR-36 instrument using data from the 1999 Large Health Survey of Veteran Enrollees (Veterans Health Study) (Iqbal, 2009). Higher PCS and MCS scores reflect better quality of life. The VR-12 was self-administered at baseline, clearing, and during post-pairing follow-up visits at 3, 6, 9, 12, 15, and 18 months. The timeframe for the VR-12 was the past four weeks.

ii. Secondary outcome measures

Six secondary outcomes measures were chosen to assess mental health.

Pittsburgh Sleep Quality Index (PSQI). The PSQI was used to assess sleep quality. It is a 24-item self-administered survey used to assess sleep-related problems during the past month (Buysse, et al., 1989) of which 19 items are completed by the participant, and five items are completed by a bed partner or roommate. The five items answered by a bed partner or roommate are used as clinical information and are not included in scoring. The items completed by the participant are grouped into seven components: (1) sleep quality, (2) sleep latency, (3) sleep duration, (4) habitual sleep efficiency, (5) sleep disturbances, (6) Use of sleep medication, and (7) daytime dysfunction. Each of the seven components are weighted equally on a 0-3 scale with 0 (better) to 3 (worse). The seven component scores are summed to yield a global score, with a range of 0-21 such that higher scores indicate worse sleep quality. The PSQI was administered at baseline, clearing, and during post-pairing follow-up visits at 3, 6, 9, 12, 15, and 18 months. The timeframe for the PSQI was the past month.

Columbia-Suicide Severity Rating Scale (C-SSRS). The C-SSRS was used to assess suicidal ideation (Oquendo, et al., 2003). It asks questions about suicidal ideation, intensity of ideation, and suicidal behavior. Each item is considered to be a discussion probe; thus, it must be administered by a trained administrator in interview format. Determination of the presence of suicidality depends on clinical judgment. Scoring was dichotomized as the presence or absence of suicidal behavior or ideation based upon a “Yes” response to any one of the five suicidal behavior or five suicidal ideation questions. The C-SSRS was administered at screening, clearing, and during post-pairing follow-up visits at 3, 6, 9, 12, 15, and 18 months. The timeframe for the C-SSR was since the last visit.

PTSD Civilian Checklist 5 (PCL-5). The PCL-5 was used to assess change in PTSD symptoms. It is a 20-item self-report measure that assesses the 20 DSM-5 symptoms of PTSD. Each symptom is scored on a scale of 0 (not at all) through 4 (extreme). A total symptom severity score is calculated by summing the scores for each of the 20 items. Scores can range from 0 to 80, with higher scores representing greater symptom severity. The recommended minimum change in score for determining whether an individual has responded to treatment is 5 points, while the recommended minimum change to determine if improvement is clinically meaningful is 10 points (Weathers, et al., 2013). The PCL-5 was administered at screening, clearing, and

during post-pairing follow-up visits at 3, 6, 9, 12, 15, and 18 months. The timeframe for the PCL-5 was the past month.

Patient Health Questionnaire (PHQ-9). The PHQ-9 was used to assess severity of depression (Kroenke & Spitzer, 2002) and consists of 9 questions that are answered on a scale from 0 (not at all) to 3 (nearly every day). The total score is calculated by adding together the symptom ratings for each of the 9 questions so that scores range from 0 to 27 (higher scores represent greater severity). The PHQ-9 was self-administered at baseline, clearing, and during post-pairing follow-up visits at 3, 6, 9, 12, 15, and 18 months. The timeframe for the PHQ-9 was the last two weeks.

Dimensions of Anger Reactions (DAR). The DAR is a seven-item scale that assesses anger disposition directed to others (Forbes, et al.,2004). Participants are asked to indicate the degree to which each statement describes their feelings and behavior on an 8-point scale ranging from 0 (not at all) to 8 (exactly so). Scores are totaled yielding a range of 0-56, with higher scores indicating greater anger disposition. The DAR was self-administered at baseline, clearing, and during post-pairing follow-up visits at 3, 6, 9, 12, 15, and 18 months. The timeframe for the DAR was the past four weeks.

E. Procedures

i. Recruitment

Participants were recruited using three primary strategies: 1) IRB-approved presentations about the study given to mental health providers at each VA site during which the study was described and providers were encouraged to refer potentially eligible Veterans, 2) Emails with IRB-approved study recruitment fliers sent to mental health providers at each VA site asking them to encourage potentially eligible Veterans to inquire about the study, and 3) IRB-approved flyers and brochures distributed directly to potential participants following mental health visits and placed in mental health clinic waiting areas and at meeting locations of Veteran-centric interest groups and organizations. The study fliers provided contact information for the local study team.

Additional local recruitment strategies included: 1) Vendor and other external professionals' referrals of potential participants via provision of study team contact information, IRB approved flyers/brochures and/or in-service presentation, 2) Advertising via social media outlets (i.e., VA Facebook page, VA Twitter account), VA related newsletters (internal and external), and VA closed circuit TV (all content was limited to language included in the approved study brochure and/or flyer) and, 3) Information booths set up at local community events with a focus on Veteran populations.

Potential participants could be self-referred, referred by a local mental health provider via CPRS or other contact, or referred by a dog vendor or other external professional following contact by an interested individual. If the potential participant was informally referred, they were required to obtain a formal study referral from their mental health provider.

ii. Preliminary Screening Process

Preliminary screening procedures occurred prior to scheduling the initial assessment visit, referred to as "screening". First, potential participants underwent a telephone screening interview

using an IRB-approved script. They were asked about their PTSD symptoms, whether they were enrolled in VA mental health services, whether they owned dogs, cats or other household pets, whether they had children in their home, and about their current living arrangement. Second, a member of the study team examined the potential participant's electronic medical record to review applicable eligibility requirements. Third, individuals who met the inclusion/exclusion criteria at that point and who were interested in the study were asked to obtain a referral letter from their VA mental health provider to be shared with the study team at or prior to the Screening Visit.

iii. Formal Screening Process

Following the receipt of the mental health referral letter form, the potential participant attended an in-person clinic Screening Visit at the local VA study site. At the start of the screening visit, participants provided written informed consent and signed a Health Insurance Portability and Accountability Act of 1996 (HIPAA) authorization form. Participants were also sent a hard copy of the informed consent form by mail in advance of the visit, so they could come to the visit prepared with questions as needed. At the completion of the informed consent process, a short demographic interview was administered. Eligibility for study participation was determined at a qualifying clinic visit using the Clinician Administered PTSD Scale (CAPS) and the Mini-International Neuropsychiatric Interview (MINI). CAPS is the gold standard for the diagnosis of PTSD and Table H summarizes the criteria used (Weathers, et al., 2013). It is a well-validated structured clinical interview that measures the intensity and frequency of the 20 DSM-V PTSD symptoms. It includes questions which target the onset and duration of symptoms, subjective distress, impact of symptoms on social and occupational functioning, improvement in symptoms since previous CAPS (if applicable), overall PTSD severity and specifications for the dissociative subtype. The CAPS updated for DSM-V produces a dichotomous assessment of PTSD. A member of the research team trained in administering the CAPS completed the assessment. If the CAPS criteria were met, measures to assess exclusionary symptoms were completed.

Table H. CAPS criteria for diagnosis of PTSD

Criterion	Description
A: stressor (one required)	The person was exposed to: death, threatened death, actual or threatened serious injury, or actual or threatened sexual violence, in the following way(s): direct exposure, witnessing trauma, learning a relative or close friend was exposed to trauma, or indirect exposure to aversive details of trauma usually related to occupation.
B: intrusion symptoms (one required)	The traumatic event is persistently re-experienced in the following way(s): unwanted upsetting memories, nightmares, flashbacks, emotional distress after exposure to traumatic reminders, physical reactivity after exposure to traumatic reminders.
C: avoidance (one required)	Avoidance of trauma-related stimuli after the trauma, in the following way(s): trauma-related thoughts or feelings or trauma-related external reminders.
D: negative alterations in cognitions and mood (two required)	Negative thoughts or feelings that began or worsened after the trauma, in the following way(s): inability to recall key features of the trauma, overly negative thoughts and assumptions about oneself or the world; exaggerated blame of self or others for causing the

	trauma; negative affect, decreased interest in activities, feeling isolated, or difficult experiencing positive effect.
E: alterations in arousal and reactivity (two required)	Trauma-related arousal and reactivity that began or worsened after the trauma, in the following way(s): irritability or aggression, risky or destructive behavior, hypervigilance, heightened startle reaction, difficulty concentrating, or difficulty sleeping.
F: duration (required)	Symptoms last for more than 1 month.
G: functional significance (required)	Symptoms create distress or functional impairment (e.g., social, occupational).

Next, the MINI was conducted during screening for eligibility and was used to assess the active psychosis, delusions, or dementia and other Axis-I disorders according to DSM–V criteria. Initially, a trained interviewer using the MINI screen questionnaire assessed each subject. If a potential DSM-V disorder was identified via the screen, the clinician administered the corresponding module of the complete MINI interview. The presence of alcohol use disorder was assessed by the MINI, and an active diagnosis of alcohol use disorder, moderate or severe, was an exclusion criterion.

The Columbia-Suicide Severity Rating Scale (C-SSRS) was also administered to determine suicide ideation; individuals who displayed signs of active suicidal intent were excluded. A full description of the C-SSRS is provided in Section D. Outcome Measures.

Upon meeting all eligibility requirements, a home check for dog safety was scheduled. During this home visit, the potential participant's home was assessed to determine whether it was accessible and safe for both the study team and a dog. Factors examined include accessibility to outdoor space, fencing around a yard (if one was present), evidence that all doors from the home to the outside closed securely, and assurance that all household chemicals and materials that were potentially harmful if ingested could be kept way from the dog. If the home was accessible to the study team but did not meet all suitability or safety criteria, potential participants were given up to three months to fix the issues, at which time a follow-up home visit took place. Form 5 was used to evaluate the safety of the home (all forms are available at https://www.research.va.gov/programs/animal_research/PTSDstudy.cfm).

iv. Home Visit with Baseline Assessment (Baseline 1)

If all criteria above were met, during the same visit baseline outcomes assessments were completed in the following order: WHO-DAS 2.0, PCL-5, PSQI, VR-12, PHQ-9, and DAR. All assessments were completed in pen and paper form by the participant.

v. Computer Randomization and Blinding

On completion of baseline testing, a member of the study team called the Interactive Touch Tone Randomization System (ITTRS) to randomize the participant to a dog type (SERV or EMOT). A block randomization scheme created by the Perry Point Cooperative Studies Program Coordinating Center was used to randomize participants within site and vendor (stratification variables) into two treatment groups. A random sequence of block sizes of 2 and 4 were used to reduce the chances of guessing future allocations.

The participant, local study team, and dog vendor remained blinded to the assignment until later in the protocol. Randomization was conducted centrally by the study coordinating center using ITTRS. Random assignments to the intervention groups were generated by SAS 9.3, a statistical software using a random block scheme stratified by site. Once eligibility for a Veteran was confirmed, a member of the study team called the ITTRS, which then generated the randomization assignment. The local study team and the participant were blinded to the group assignment during the study observation period. Only the members of the coordinating site data collection team and members of the contract management team were informed of the assigned intervention. This was necessary so that a dog vendor could be assigned, and training of a dog for that participant could be coordinated.

vi. Assignment of dog vendor

Three selected vendors provided both SERVs and EMOTs. Following randomization, a vendor was assigned based on dog availability by the contract management team. Subject to limitations in dog supply from individual vendors over time, the contract management team attempted to keep the vendor assignments for participants from each study site roughly balanced among the three dog vendors to prevent any bias in vendor/study site assignments. Once the vendor assignment was made, the vendor conducted a dog-matching interview with the participant. The details of the blinding procedures built into the study are described in the next section.

vii. Observation Period

The Observation Period started with the Baseline Home Visit (Baseline 1) and ended with the Home Clearing Visit. Following the completion of the Baseline Home Visit, there was a three-month minimum observation period that ended with home clearing visit, which was scheduled once a dog became available. As noted above, during this period the Veteran and local study team were blinded to the intervention group to which the participant was randomized. At the start of the observation period, the participant was provided with contact information by the study team for their assigned vendor to set up a dog-matching interview. During the observation period, the vendors interviewed the participants to gain a sense of the person's physical traits and lifestyle (i.e. tall, athletic man with no physical handicaps that enjoys playing sports versus petite woman who is right-handed, walks with cane, and likes to watch movies). Once sufficient information was obtained about the participant, the vendor asked the VA Contracting Officer's Representatives to reveal the dog type assignment for that participant. The vendor then selected a dog(s) that matched the participants personality and lifestyle and began training these dogs according to participant's randomization group. The vendor did not have further contact with the participant until the participant learned later of their assigned dog type and vendor at the home clearing visit, which followed the clinic clearing visit. The study team was blinded to the dog assignment until participant learned the dog type assignment at the clearing visit. Also, during the observation period, the participant completed a dog care course. The course was specially designed for this study and accessed through via the Collaborative Institutional Training Initiative (CITI) website (https://about.citiprogram.org/en/homepage/). The course included information about dog health issues and when to seek medical attention, general care and feeding of dogs, recognition and prevention of dog aggression, financial burden associated with having a dog both during and after the study, the differences between SERV and EMOTs, and legal rights of SERV and EMOT

owners. The entire VA Dog Care Course may be viewed at: https://www.research.va.gov/programs/animal_research/PTSDstudy.cfm.

viii. Clinic Clearing Visit

Once the dog assigned by the vendor to the participant had been proofed and accepted by VA (see 2. Contract Requirements) and was ready for the participant, a clinic visit took place during which a second set of baseline assessments (Baseline 2) was completed. Identical measures and procedures were used as previously described, and the participant completed a Dog Knowledge Test (also available at course link above) to ensure he/she understood and adequately recalled the content of the dog care course. Participants who scored <80% correct on the test received additional face to face education from the local dog trainer. At the Clinic Clearing Visit, outcome measures were assessed as an internal control to enable comparison of clearing versus baseline and to determine if there were any outcome changes over time prior to pairing.

ix. Home Clearing Visit

Following the completion of the Clinic Clearing Visit, a second home visit was conducted to reconfirm that the home was still suitable for a dog. If all criteria were met, the participant and local study team were then unblinded to the type of dog the participant would receive. This visit was the end of the Observation Period.

x. Interventions

1) Provision of a PTSD SERV

For this study, SERVs were required to initially pass the American Kennel Club (AKC) Canine Good Citizen Test and then pass the Assistance Dogs International (ADI) Public Access Test (Assistance Dogs International, 1997). SERVs were taught to perform five tasks specific to PTSD (e.g. block, lights, sweep, bring, and behind); these tasks were selected by a team of mental health professionals with expertise in PTSD. For a discussion of additional considerations in selecting these tasks, see 2. Contract Requirements and the 5. Discussion.

2) Provision of an EMOT

Like SERVs, EMOTs had to be well-behaved, and well-socialized to people and other animals, but they were not taught specific tasks to mitigate PTSD symptoms. For this study, EMOTs were required to pass the AKC Canine Good Citizen Test and the more advanced AKC Community Canine Test, which is much less stringent than but shares some components with the ADI Public Access Test used for the SERVs. For more details see 2. Contract Requirements.

xi. Pairing

The dog-pairing process varied based on the type of dog assignment. Participants who received a SERV traveled to the vendors' facility where they received training on handling their assigned SERV. Participants who received an EMOT were trained at their home or a nearby location by the local VA dog trainer. SERV training was by necessity longer and more intensive than EMOT training because SERVs have public access privileges and the SERV must be under the control of the handler at all times. In contrast, participants who received EMOTs only needed

to be competent in basic dog handling skill, such as for a pet dog. For more details see 2. Contract Requirements.

xii. Post Pairing Monitoring Visits

One week after pairing, the local VA dog trainer conducted a home visit to verify that the pairing process was successful. During this visit, the local dog trainer collected data regarding dog health and behavior and interviewed the participant to determine whether he/she had any concerns and challenges that needed to be addressed.

Two weeks after pairing, the participant was contacted for a second time by the local VA dog trainer. If there were no concerns at the one-week follow-up and there were no children under age 10 years living in the home, the contact was completed by telephone. If there were concerns at the one-week follow-up, or if the participant had any children between 5 and 10 years old living in the home, the visit was completed in-person at the participant's home. Once again, data regarding dog health and behavior, and participant concerns and challenges was collected.

One month and two months after pairing, the local dog trainer conducted additional home visits/contacts with the participant using the same protocols as described above for the one-week and two-week follow-ups, respectively. Once again, if there were any children between 5 and 10 years of age living with the participant, then home visits were required.

xiii. Post Pairing Outcome Visits

At 3, 9, and 15 months after pairing, participants attended a study appointment at the local VA study site. During these visits, the primary and secondary outcome assessments were administered using the order and protocol described in the *iv. Home Visit with Baseline Assessment* section. In addition, the C-SSRS was administered in interview format at each visit to monitor for suicidal intent, and the CAPS was completed at the 15-month visit.

At 6, 12, and 18 months after pairing, a home visit was conducted by the local study team at which the primary and secondary outcome assessments were administered using the order and protocol described in the *iv. Home Visit with Baseline Assessment* section outlined previously. Data regarding dog health and behavior, and participant concerns and challenges were also collected. In addition, the C-SSRS was administered in interview format at each visit to monitor for suicidal ideation and intent.

At the 18-month visit, an Exit Interview was conducted by a trained interviewer during which the participant was asked whether he/she wanted to keep the dog, the reasons why, the positive and negative aspects of having a dog long term, the ways in which the dog helped with symptoms of PTSD, the specific service dog tasks actually used, the frequency with which each task was used, what other tasks participants would have liked the dog to be trained to do, the ways in which the dog has impacted quality of life, ways in which the dog had influenced interpersonal relationships, and whether the participant thought others would say their dog had helped them. There were two versions of these interviews because questions were tailored to either SERVs or EMOTs (e.g. the EMOT interview did not address service dog tasks).

xiv. Veterinary checks

To ensure that the dogs began and remained healthy throughout the study, participants were required to take the dog to a veterinarian for a thorough health check at 1-week, 6-months, 12-months, and 17-months post-pairing. Completed forms were reviewed by VA Veterinarians. When needed, VA Veterinarians followed up with a local veterinarian to authorize additional testing and/or treatment to ensure all study dogs received excellent veterinary care.

xv. Study Stipends

Participants were compensated $25 for each clinic visit and $10 for each home visit completed. In addition, after being paired with a dog, they received a stipend of $75 per month for dog care (food, toys, bedding, etc.), a coupon for dog food, and an insurance policy to cover the costs of veterinary care for the dog for the duration of their enrollment in the study (see 2. Contract Requirements).

xvi. Data and Safety Monitoring

A Data and Safety Monitoring Committee, comprised of individuals with expertise in statistics, veterinary medicine, and PTSD, was established to monitor study progress. The committee was tasked with monitoring study progress, recruitment, trial safety, protocol adherence, and data quality. The committee decided that study safety data, rather than results of interim analyses, would be used to determine whether the study should be terminated at any point. Model testing was performed but an interim analysis was not.

xvii. Adverse Events - Definitions and Reporting

The study was not designed and powered to analyze harms data as an endpoint. Information regarding adverse events (AEs) and serious adverse events (SAEs) for participants and study dogs were elicited with open ended questioning by the study teams (e.g. study forms 26, 26a, 27, 27a, 28, and 28a) at every participant contact throughout the conduct of the trial. Immediate reviews of incoming data were completed by the Adverse Event Specialist, a regulatory pharmacist, throughout the trial, as well as aggregate safety data being monitored by the DMC and study leadership periodically. Adverse Event Coders, who were registered, clinical nurses, classified these events according to MedDRA and sponsor coding convention. The Medical Dictionary for Regulatory Activities (MedDRA) was developed by the International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH); it is a well-recognized resource for highly specific, standardised medical terminology The definitions of adverse event (AE) and Serious Adverse Events (SAE) used in the study were based upon ICH definitions. An AE was defined as “any untoward medical occurrence in a clinical investigation subject that is subjected to one of the study treatments that does not necessarily have to have a causal relationship with the treatments”, while a SAE was defined as “any event that results in death, is life threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability or incapacity, is a congenital anomaly/birth defect, or any other condition that, based upon medical judgment, may jeopardize the subject and require medical, surgical, behavioral, social or other intervention to prevent such an outcome.” The study involved both humans and dogs, thus AEs and SAEs pertained to either or both. The Medical Dictionary for Regulatory Activities (MedDRA) version 20.0 nomenclature (MedDRA 2017) was used to code SAE and AE events.

Reporting of adverse events was conducted in accordance with the Department of Health and Human Services Office for Human Research Protections guidelines. AE reporting began at the time of enrollment and ended 30 days after the participant ended their study participation. All SAEs were reported to the IRB. Further, potential SAEs involving dog deaths, dog bites, or participant deaths were reported immediately to the study leadership team within 12 hours of the local study team becoming aware of the event. Only AEs related to or possibly related to the study intervention for the participant, participant family members, or the study dog were collected and recorded.

xviii. Study Dog Removals and Replacements

In some cases, study dogs were either temporarily or permanently removed from the care of the participant. This happened for several reasons including:

- A bond between the participant and his/her dog was not established. The lack of bonding usually becomes clear within the first 2 weeks of dog ownership. In the case of failed bonding, a VA dog trainer intervened and informed the contracting team, who then arranged for the dog to be returned to the vendor. If a returned dog could not be assigned to another participant, the vendor arranged to adopt the dog into a suitable home.
- A dog developed disqualifying health or behavioral problems at some point after pairing.
- Temporary absence due to hospitalization, transitional housing, etc., which may have disrupted the bonding process.
- The participant needed time away from the dog for mental health or other reasons.
- Voluntary return of the study dog by the participant.
- Involuntary removal of the study dog by the study team due to participant related disqualifying behavior.

When issues were identified that required the removal of a study dog including failure to develop an bond, site staff worked with their local LSI, local dog trainer, study Chair, National Dog Trainer, and other leadership to determine whether the dog should be temporarily or permanently removed. Arrangements were made for the participant to receive a replacement dog of the same dog type (SERV or EMOT).

Nine participants received a replacement dog, for reasons summarized in Table J. In the rare event a dog died while paired with a participant, the participant received support from the study team's mental health professional and his/her own mental health provider was informed. Grief counseling for the participant was also provided as needed. In the event of a dog death resulting from natural causes, illness, or accidental injury, a decision was made to provide a replacement dog, if the participant so chose. In this instance, the participant received the same dog type as they previously had. Data collection continued on the same timeline as prior to the dog's death. If the Veteran refused the replacement dog, study staff determined if the participant was eligible to remain in the study to complete non-dog related visits (per the Intent to Treat (ITT)

design). If participants were no longer eligible or were eligible but no longer wished to remain in study follow-up, they were withdrawn from the study.

F. Data Analysis

Descriptive analyses included frequencies (percentages) and means (standard deviations) of demographics and mental health, quality of life and limitation outcomes overall and by treatment group, SERV versus EMOT. Bivariate analyses comparing participant characteristics by center and treatment employed chi-square analyses (or Fisher's Exact) for categorical variables and two-sample t-tests (or Wilcoxon rank-sum) for continuous variables. All statistical tests were 2-sided using a 5% significance level, and all analyses were performed using SAS version 9.4.

The values used for the minimal clinically important difference (MCID) in the WHO-DAS 2.0 and VR-12 were informed largely by researchers experienced in PTSD studies. To the degree that the cut points are 'clinically' important is the subject of much debate as a MCID for the VR-12 and WHODAS 2.0 among PTSD populations is not well documented in the literature. However, the WHODAS 2.0 has a rich history of being utilized in over 810 studies representing 94 countries (Stefano, et al., 2017). Factor analyses (Axelsson, et al., 2017) found high internal consistency, acceptable test-retest reliability, and sensitivity to change in the primary psychiatric conditions of anxiety and perceived stress with "a convincing gradient in change effect size over the nonimproved versus slightly improved versus much improved strata." As well, Marx, et al., 2015 supported the use of WHODAS 2.0 in disability assessments as a replacement of the Global Assessment of Functioning (GAF) based on analyses of 177 Veterans seeking disability compensation for PTSD. Additionally, the VR-12 scores are standardized using a T-score metric with a mean of 50 and a standard deviation of 10 and has been represented in the literature by over 150 articles (Schalet, et al., 2015). To calculate sample size, data from two on-going CSP studies (as of 2013) were used as an estimate of WHO-DAS 2.0 mean scores and SD. Data from a study used to assess outcomes in participants who participated in a mindfulness-based stress reduction program were used as the VR-12 PCS and MCS mean and SD (Kearney, et al., 2012). The MCID was set at a 10-point difference between groups in the WHO-DAS 2.0 total score and 15% difference between groups for the VR-12 PCS and MCS based on consensus of the study's planning committee. Additional detail can be found in the study's design paper (Saunders et al., 2017).

i. Baseline and Clearing comparisons

The study assessed measures at two time points prior to pairing: baseline (prior to randomization) and clearing (after the observation period but before pairing). To examine changes between these two time points, baseline and clearing, analyses included the paired t-test (or Wilcoxon signed-rank test) and McNemar's test.

ii. Mental Health Outcomes

The primary mental health outcomes included the WHO-DAS 2.0, which assesses overall disability, and the VR-12, which assesses health-related quality of life (PCS for physical health, MCS for mental health). Secondary outcomes included PTSD symptoms (PCL-5), depression (PHQ-9), sleep (PSQI), and anger (DAR). We also measured suicidality using the C-SSRS.

Finally, we measured DSM-5 psychiatric diagnosis at baseline, per the MINI, but this measure was not expected to change over time and was not measured at follow-up. The primary outcome measures included total scores for the WHO-DAS, VR-12 MCS, and VR-12 PCS. Secondary outcome measures included total scores for the PCL-5, PHQ-9, and PSQI. Total score for DAR and the SBI of the C-SSRS were also used. All measures were continuous except for SBI (binary). Time points of first and secondary outcome measures is detailed in Figure F. All primary and secondary objectives were to assess change in measures over time between groups. Analyses included measures assessed at baseline, and 3, 6, 9, 12, 15, and 18 months.

For all the mental health outcomes except suicidality, a traditional linear repeated measures mixed model was then used to determine changes over time between the SERV and EMOT groups with gender, center and the baseline score of the outcome measure included as covariates, as well as a time by treatment group interaction (with time as a categorical variable) and using an unstructured covariance structure to model within-subject variation. Adjustment using center, gender, and baseline scores were prespecified. Center was a stratification factor, and gender was included to account for any potential confounding gender effects. Using the same set of covariates, an additional analysis using a linear repeated measures mixed model with random intercepts was also employed modeling between-subject variation. The random intercept was based on the participant and corrects the standard errors given the repeated observations for each participant. Suicidality (per C-SSRS) was examined using a generalized linear mixed model, assuming a binomial distribution and logit link. Linear contrasts testing for a difference between groups across time and at 18 months employed effect coding.

iii. Additional Models

The study team recognized there were several logistical challenges of pairing participants with a study dog that did not allow for immediate pairing following randomization, such as ensuring an appropriate match of participant and dog, the availability of study dogs, training, and home environment considerations; therefore, a conscious decision was made to incorporate an observation or waiting period to ensure the safety of both participants and study dogs. Analyses of all outcome measures were based on the per-protocol population (PP) of randomized and paired participants, which was defined as the population of participants who were paired with a dog based on their initial randomization assignment and included data collected after any replacement dogs were provided to participants. Consequently, the PP population may be considered a modified intent-to-treat (mITT) population as it is comprised of a subset of the participants randomized (ITT population) and maintains the randomization structure but excludes individuals in a justified way, such as for ineligibility reasons, following randomization or for never starting treatment (paired with a study dog). Participants in PP were followed for outcome measures after pairing regardless of whether the study dog remained paired with the participant or was removed and/or replaced. An additional dataset was derived from the PP dataset by removing any data collected after a replacement dog was provided (the Per Protocol [Replacement Dog] Data Removed, or PPDR). Only nine participants received a replacement dog (see Table J). All models were re-run with the PPDR dataset to examine whether the results were sensitive to dog replacements. Other models were completed to examine time and treatment effects.

iv. Attrition and Missing Data Analyses

Unbalanced dropout, also known as differential attrition or differential dropout, can introduce bias into the analysis. Potential factors that could be associated with differential attrition were examined using bivariate analyses and logistic regression, including demographic and clinical covariates from baseline. The impact of missing data on outcome results was assessed using the Fully Conditional Specification (FCS) multiple imputation method.

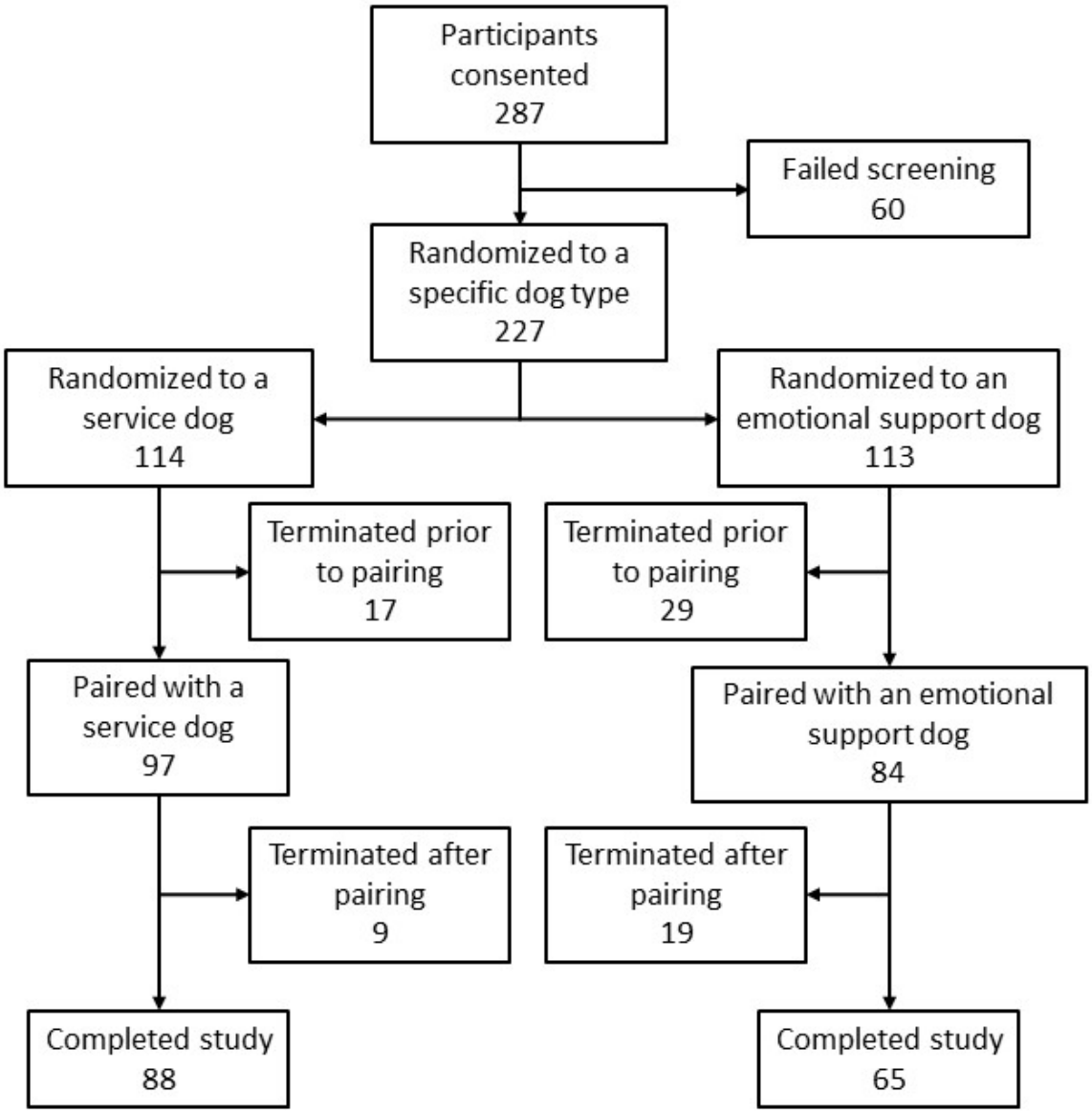
4. Results

A. Enrollment, Randomization, and Pairing

In this study, participants randomized and not paired with a dog were not followed, and therefore, no primary or secondary outcome information was collected on these participants. Imputing 18 months of follow-up information solely based on baseline data was not reasonable as it potentially introduces a large amount of error, limits interpretation and creates a challenge from which to draw conclusions. If these participants who did not actually receive any treatment were included with those receiving treatment, it may result in a more conservative estimate of treatment effect, introduce heterogeneity (e.g., noncompliant and dropout participants mixed with compliant participants in the final analysis), and thus indicate very little about the efficacy of the treatment and make interpretation more challenging. Further, mITT is an acceptable analysis in RCTs involving more complex study designs such as this one. However, ITT analyses were performed, and found no substantial differences from that reported in this monograph observed for the study's primary outcomes; therefore, the ITT population with all missing data imputed was not included.

As noted in 3. Methods, recruitment began December 2014 and continued through June 2017 when the recruitment goals had been met. All participants had been paired with a study dog by December 2017; the last participants exited the study in June 2019. A total of 287 participants were consented and enrolled in the study; 227 of the 287 participants met eligibility criteria. Of the 227 eligible participants, 114 (50.2%) were randomized to receive a SERV, and 113 (49.8%) were randomized to receive an EMOT as shown in Figure I.

Figure I. Summary of Randomization and Pairing



Forty-six (20.3%) randomized participants were terminated from the study prior to pairing (17 in the SERV intervention group and 29 in the EMOT intervention group). The remaining randomized participants (n=181) were paired with a study dog – 97 (53.6%) with a SERV, and 84 (46.4%) with an EMOT after a median waiting period of 5.2 months (range 3.0 – 12.9 months). Nine participants, 3 (3.1%) in the SERV group and 6 (7.1%) in the EMOT group, received a replacement dog at some point after the initial dog pairing. Table J lists the reasons replacement dogs were needed. Among paired participants, 9 participants (9.3%) of 97 paired with a SERV

terminated early, and 19 participants (22.6%) of 84 paired with an EMOT terminated early. Replacement dogs were always the same type of dog as the original dog (a SERV would replace a SERV, and an EMOT would replace an EMOT). The impact of this differential dropout is assessed in a subsequent section (Section G. Attrition Analyses).

Table J. Reasons replacement dogs were needed

Reason Replacement Dog was Needed	Dog type
Veteran was required to seek new residence, and the transition back and forth from the vendor foster family was deemed excessively disruptive for the dog.	SERV
Participant reported that dog displayed some aggressive tendencies toward people, but behavior could not be reproduced by VA trainers.	SERV
Dog experienced medical issues (including knee surgery) impeding dog's ability to perform service dog tasks.	SERV
Dog displayed aggressive behavior toward another dog and had leash-pulling issues.	EMOT
Dog displayed signs of separation anxiety with destructive behavior and became overstimulated outside the home and ignored commands.	EMOT
Dog did not adhere to basic commands and was a flight risk.	EMOT
Incompatible dog placed with Veteran due to local error (dog too large for small person; dogs were switched)	EMOT
Incompatible dog placed with Veteran due to local error (dog too small for large person; dogs were switched)	EMOT
Dog displayed aggression (bit Veteran and Veteran's partner; (Level 2 on Dunbar Scale) and did not respond to commands. This was reported to the IRB as an adverse event. *Note:* No children sustained a dog bite during this clinical trial.	EMOT

i. Withdrawals

Withdrawals were expected to occur over the course of the study. A description of demographic characteristics between participants who were randomized but not paired with a dog and those who were paired with a dog is shown in Table K. As shown in Table L, a total of 46 participants withdrew (14 were involuntary) *before* pairing with a dog; of those 46 participants, 29 were in the EMOT group and 17 were in the SERV group. The number of withdrawals that occurred *after* pairing was smaller but was still higher in the EMOT group (19) as compared to SERV group (9).

The most common reasons for participants being withdrawn from the study *before* receiving their EMOT or SERV were a change in eligibility status and moving out of the area, which prevented any further follow-up and required withdrawal (see Table M). Eleven participants in the EMOT group were withdrawn due to a change in eligibility status. The specific reasons were: unwilling to accept randomization assignment (n=6), participant behavioral concerns (n=2), unable to adequately care for the dog (n=2), and household member would not accept the dog (n=1). Participants in the SERV group (n=3) were withdrawn for hospitalization related to mental health, unwilling to accept randomization outcome, and unable to adequately care for dog.

Two participants in the EMOT group were withdrawn due to SAEs; one participant experienced depression and suicidal ideation related to PTSD exacerbation and the other suffered

a substance abuse relapse after a long period of sobriety (see ii. Serious Adverse Event (SAE) and Adverse Event (AEO findings).

As shown in Table N, the reasons for withdrawals in the EMOT group *after* pairing varied widely but the two most common reasons were the participant's family decided to withdraw (n=4) and not able to care for the dog (n=3). Two participants in the EMOT group indicated they wanted their dogs for protection, which was not consistent with contract requirements or VA expectations for EMOTs. In contrast, the most common reason for withdrawal in the SERV group was the participant could not be located, which means their SERVs had been returned and VA withdrew these participants from the study (e.g. non-voluntary withdrawal). During the study, two study dogs died (one confirmed death and one presumed death) as a result of being hit by motor vehicles. In the case of an EMOT's death, the dog escaped a fenced yard through an unsecured gate and was fatally struck. The other death was the result of the participant walking the SERV off-leash; the SERV bolted and could not be found. A few days later, VA was informed that a dog matching the description of the SERV was found deceased following an apparent motor vehicle collision. However, microchip confirmation of the dog's identity was not possible.

The *raw number* of participant withdrawals both before and after pairing were higher in the EMOT group versus the SERV group. As shown in Table L, 1.7 and 2.1 times more EMOT dog pairs randomized were withdrawn before and after pairing, respectively, than SERV dog pairs. And overall, 1.9 times more EMOT pairs were withdrawn than SERV pairs (48 EMOT pairs, 26 SERV pairs).

A "corrected" withdrawal rate after pairing was also analyzed in terms of the *percentage of each dog pair type withdrawn versus the number of starting pairs*, to correct for the fewer EMOT (84) versus SERV (97) pairings (caused by higher withdrawals before pairing in the EMOT group). Using this approach, 22.6% (19 out of 84) EMOT pairs were withdrawn versus 9.3% (9 out of 97) in the SERV group, giving 2.4 times higher incidence of withdrawals in the EMOT versus SERV group after pairing by this analysis method.

So, the withdrawal rate before and the corrected rate after pairing went from 29.7% to 22.6% (23.9% drop) in the EMOT group and went from 14.9% to 9.3% (37.6% drop) in the SERV group. The larger reduction in withdrawal percentages in the SERV group provides additional circumstantial evidence that potentially participant satisfaction with SERV dogs was higher versus EMOT dogs, although underlying perceptions as described above could also be involved.

Considering the various approaches to analyzing the data, it is reasonable to conclude that participants assigned to an EMOT dog were overall about twice as likely to withdraw from the study than participants assigned to a SERV dog.

Table K. Demographics for participants randomized but not paired with a dog and participants paired with a dog

	Statistics	Paired (n=181)	Not Paired (n= 46)	Total (n=227)
Age (years)	N	181	46	227
	Mean (SD)	50.6 (13.61)	48.6 (13.97)	50.2 (13.67)
	Median	51.0	48.0	51.0
	Min, Max	22, 79	26, 69	22, 79

Gender	N	181	46	227
Male	N (%)	145 (80.1)	32 (69.6)	177 (78.0)
Female	N (%)	36 (19.9)	14 (30.4)	50 (22.0)
Race	N	181	46	227
American Indian or Alaskan Native	N (%)	3 (1.7)	1 (2.2)	4 (1.8)
Asian	N (%)	2 (1.1)	0 (0.0)	2 (0.9)
Black, or African-American	N (%)	22 (12.2)	6 (13.0)	28 (12.3)
Native Hawaiian or Pacific Islander	N (%)	1 (0.6)	0 (0.0)	1 (0.4)
White	N (%)	120 (66.3)	31 (67.4)	151 (66.5)
Unknown	N (%)	1 (0.6)	0 (0.0)	1 (0.4)
Other	N (%)	1 (0.6)	1 (2.2)	2 (0.9)
Multiple Races	N (%)	31 (17.1)	7 (15.2)	38 (16.7)
Ethnicity	N	181	46	227
Hispanic	N (%)	12 (6.6)	3 (6.5)	15 (6.6)
Not Hispanic	N (%)	165 (91.2)	41 (89.1)	206 (90.7)
Unknown	N (%)	4 (2.2)	2 (4.3)	6 (2.6)
Marital Status	N	181	46	227
Married	N (%)	69 (38.1)	12 (26.1)	81 (35.7)
Co-habitating	N (%)	9 (5.0)	0 (0.0)	9 (4.0)
Widowed	N (%)	5 (2.8)	2 (4.3)	7 (3.1)
Never Married	N (%)	24 (13.3)	10 (21.7)	34 (15.0)
Divorced	N (%)	65 (35.9)	17 (37.0)	82 (36.1)
Separated	N (%)	9 (5.0)	5 (10.9)	14 (6.2)
Education Level	N	181	46	227
< High School Diploma	N (%)	3 (1.7)	1 (2.2)	4 (1.8)
High School Diploma/GED	N (%)	30 (16.6)	8 (17.4)	38 (16.7)
Some College Credit	N (%)	72 (39.8)	16 (34.8)	88 (38.8)
Associate Degree	N (%)	31 (17.1)	4 (8.7)	35 (15.4)
Bachelor’s Degree	N (%)	23 (12.7)	10 (21.7)	33 (14.5)
Master’s Degree	N (%)	19 (10.5)	6 (13.0)	25 (11.0)
Ph.D. or Professional Degree	N (%)	3 (1.7)	1 (2.2)	4 (1.8)
Income Level	N	181	46	227
< $10,000	N (%)	10 (5.5)	1 (2.2)	11 (4.8)
$10,001 - $20,000	N (%)	25 (13.8)	7 (15.2)	32 (14.1)
$20,001 - $30,000	N (%)	25 (13.8)	9 (19.6)	34 (15.0)
$30,001 - $40,000	N (%)	29 (16.0)	8 (17.4)	37 (16.3)
$40,001 - $50,000	N (%)	29 (16.0)	10 (21.7)	39 (17.2)
$50,001 - $60,000	N (%)	28 (15.5)	4 (8.7)	32 (14.1)
$60,001 - $70,000	N (%)	19 (10.5)	3 (6.5)	22 (9.7)
> $70,001	N (%)	15 (8.3)	3 (6.5)	18 (7.9)
Missing	N (%)	1 (0.6)	1 (2.2)	2 (0.9)
Walk Outside	N	181	46	227
Never	N (%)	14 (7.7)	1 (2.2)	15 (6.6)

One or time times a week	N (%)	40 (22.1)	12 (26.1)	52 (22.9)
At least once a day	N (%)	86 (47.5)	26 (56.5)	112 (49.3)
More than once a day	N (%)	39 (21.5)	7 (15.2)	46 (20.3)
Missing	N (%)	2 (1.1)	0 (0.0)	2 (0.9)
Served Outside US	N	181	46	227
No	N (%)	14 (7.7)	10 (21.7)	24 (10.6)
Yes	N (%)	167 (92.3)	36 (78.3)	203 (89.4)
Served in Combat Area	N	181	46	227
No	N (%)	47 (26.0)	12 (26.1)	59 (26.0)
Yes	N (%)	134 (74.0)	34 (73.9)	168 (74.0)
Hearing Impairment	N	181	46	227
No	N (%)	95 (52.5)	28 (60.9)	123 (54.2)
Yes	N (%)	85 (47.0)	18 (39.1)	103 (45.4)
Missing	N (%)	1 (0.6)	0 (0.0)	1 (0.4)
Visual Impairment	N	181	46	227
No	N (%)	149 (82.3)	33 (71.7)	182 (80.2)
Yes	N (%)	32 (17.7)	13 (28.3)	45 (19.8)
Mobility Impairment	N	181	46	227
No	N (%)	116 (64.1)	27 (58.7)	143 (63.0)
Yes	N (%)	64 (35.4)	19 (41.3)	83 (36.6)
Missing	N (%)	1 (0.6)	0 (0.0)	1 (0.4)
Alternative Therapy	N	181	46	227
No	N (%)	113 (62.4)	27 (58.7)	140 (61.7)
Yes	N (%)	68 (37.6)	19 (41.3)	87 (38.3)
Branch of Military	N	181	46	227
Army	N (%)	96 (53.0)	25 (54.3)	121 (53.3)
Navy	N (%)	29 (16.0)	8 (17.4)	37 (16.3)
Air Force	N (%)	17 (9.4)	6 (13.0)	23 (10.1)
Marines	N (%)	41 (22.7)	5 (10.9)	46 (20.3)
Coast Guard	N (%)	2 (1.1)	2 (4.3)	4 (1.8)
Merchant Marines	N (%)	0 (0.0)	0 (0.0)	0 (0.0)
National Guard	N (%)	20 (11.0)	4 (8.7)	24 (10.6)
When Served	n	181	46	227
World War I	N (%)	0 (0.0)	0 (0.0)	0 (0.0)
World War II	N (%)	0 (0.0)	0 (0.0)	0 (0.0)
Korean conflict	N (%)	1 (0.6)	0 (0.0)	1 (0.4)
Vietnam conflict	N (%)	50 (27.6)	10 (21.7)	60 (26.4)
Gulf War	N (%)	53 (29.3)	9 (19.6)	62 (27.3)
Balkans conflict	N (%)	4 (2.2)	0 (0.0)	4 (1.8)
Afghanistan conflict	N (%)	30 (16.6)	14 (30.4)	44 (19.4)
Iraq conflict	N (%)	61 (33.7)	20 (43.5)	81 (35.7)
Peace time	N (%)	38 (21.0)	11 (23.9)	49 (21.6)
Other conflict	N (%)	21 (11.6)	4 (8.7)	25 (11.0)
Work Status	n	181	46	227

Working part or full time	N (%)	51 (28.2)	14 (30.4)	65 (28.6)
Student full time	N (%)	16 (8.8)	5 (10.9)	21 (9.3)
Student part time	N (%)	5 (2.8)	1 (2.2)	6 (2.6)
Homemaker	N (%)	2 (1.1)	2 (4.3)	4 (1.8)
Retired not due to disability	N (%)	32 (17.7)	6 (13.0)	38 (16.7)
Volunteer full time	N (%)	0 (0.0)	0 (0.0)	0 (0.0)
Volunteer part time	N (%)	15 (8.3)	3 (6.5)	18 (7.9)
Disabled: unable to work due to physical disability	N (%)	60 (33.1)	16 (34.8)	76 (33.5)
Disabled: unable to work due to mental health status	N (%)	78 (43.1)	20 (43.5)	98 (43.2)
Unemployed and not seeking work	N (%)	13 (7.2)	4 (8.7)	17 (7.5)
Unemployed actively seeking work	N (%)	4 (2.2)	0 (0.0)	4 (1.8)
Other work status	N (%)	3 (1.7)	3 (6.5)	6 (2.6)

Table L. Number of participants withdrawn from study versus number of randomized, paired, and completed study, and comparison of EMOT and SERV groups

Description	**EMOT** n (% of randomized EMOT pairs)	**SERV** n (% of randomized SERV pairs)	**EMOT n/ SERV n**	**Total EMOTs & SERVs** n (% of all randomized dog pairs)
Number of dogs randomized to participant	113 (100)	114 (100)	0.99	227 (100)
Participants withdrawn prior to pairing (see Table J)	29 (29.7)	17 (14.9)	1.71	46 (20.3)
Number paired with participant	84 (74.3)	97 (85.1)	0.87	181 (79.7)
Participants withdrawn after pairing (see Table K)	19 (16.8)	9 (77.2)	2.11	28 (12.3)
Completed 18-month study	65 (57.5)	88 (77.2)	0.73	153 (67.4)

Table M. Reasons for forty-six (46) participant withdrawals from study <u>before</u> pairing.

Reasons for Participant Withdrawals Before Pairing	**EMOT** n (% of withdrawn EMOT pairs)	**SERV** n (% of withdrawn SERV pairs)	**EMOTs & SERVs** n (% of all withdrawn dog pairs)
Not able to care for dog	1 (3.4)	1 (5.9)	2 (4.3)
Moving out of area	5 (17.2)	5 (29.4)	10 (21.7)
Family decided to withdraw	2 (6.9)	3 (17.6)	5 (10.9)

Participant died	1 (3.4)	0 (0.0)	1 (2.2)
Terminated due to SAE	2 (6.9)	0 (0.0)	2 (4.3)
Change in eligibility status	11 (37.9)	3 (17.6)	14 (30.4)
Could not be located (not responsive to study team)	2 (6.9)	3 (17.6)	5 (10.9)
Obtained SERV from a non-study source	2 (6.9)	0 (0.0)	2 (4.3)
Dog vendor did not approve participant to receive dog	0 (0.0)	1 (5.9)	1 (2.2)
Concerned about receiving a large dog	1 (3.4)	0 (0.0)	1 (2.2)
Unwilling to wait for an available dog	0 (0.0)	1 (5.9)	1 (2.2)
Not ready for dog ownership	2 (6.9)	0 (0.0)	2 (4.3)
Total	**29 (100.0)**	**17 (100.0)**	**46 (100.0)**

Table N. Reasons for twenty-eight (28) participant withdrawals from study <u>after</u> pairing with a dog

Reasons for Participant Withdrawals After Pairing	**EMOT** n (% of withdrawn EMOT pairs)	**SERV** n (% of withdrawn SERV pairs)	**EMOTs & SERVs** n (% of all with-drawn dog pairs)
Not able to care for dog	3 (15.8 %)	0 (0 %)	3 (10.7 %)
Moving out of area	1 (5.3 %)	1 (11.1 %)	2 (7.1 %)
Family decided to withdraw	4 (21.1 %)	1 (11.1 %)	5 (17.9 %)
Participant died	1 (5.3 %)	0 (0 %)	1 (3.6 %)
Dog died	1 (5.3 %)	0 (0 %)	1 (3.6 %)
Change in eligibility status	1 (5.3 %)	0 (0 %)	1 (3.6 %)
Cannot be located (not responsive to study team)	1 (5.3 %)	4 (44.4 %)	5 (17.9 %)
Incarcerated	1 (5.3 %)	0 (0 %)	1 (3.6 %)
Administratively discharged	1 (5.3 %)	1 (11.1 %)	2 (7.1 %)
Busy schedule	1 (5.3 %)	0 (0 %)	1 (3.6 %)
Pairing with a replacement dog was not approved	1 (5.3 %)	0 (0 %)	1 (3.6 %)
Personal/housing issues	0 (0 %)	1 (11.1 %)	1 (3.6 %)
Noncompliance with dog ownership requirements for study	1 (5.3 %)	0 (0 %)	1 (3.6 %)
Participant did not want dog ownership responsibility and additional training	1 (5.3 %)	0 (0 %)	1 (3.6 %)
Noncompliance with requirements for study participation	0 (0 %)	1 (11.1 %)	1 (3.6 %)
Family member allergic to dog	1 (5.3 %)	0 (0 %)	1 (3.6 %)
Total	**19 (100.0)**	**9 (100.0)**	**28 (100.0)**

ii. Serious Adverse Event (SAE) and Adverse Event (AE) findings

SAEs and AEs were coded using the Medical Dictionary for Regulatory Activities (MedDRA) version 20.0 nomenclature (MedDRA 2017). Table O shows 109 SAE events in 57 participants were reported for all randomized participants (before pairing and after pairing); none

of these were related to the participants' dogs. The most common SAEs were psychiatric disorders, which occurred in 11 participants assigned to the EMOT group and 8 participants assigned to the SERV group. Based on the MedDRA preferred term, SAEs in the psychiatric disorders class were suicide ideation (12 events/10 participants - 5 EMOT versus 5 SERV), depression (3 events/3 participants – all SERV), suicide attempt (3 events/2 participants – 1 EMOT versus 1 SERV)), alcohol abuse (3 events/1 EMOT participant), and anxiety (2 events/2 participants – 1 EMOT versus 1 SERV). Alcoholism, drug use disorder, worsening of PTSD, and substance use disorder were only diagnosed in participants assigned to the EMOT group; there was one event per participant.

In contrast to the SAEs, all AEs were either directly or indirectly related to the participants' dogs and all AEs occurred in participants assigned to the EMOT group (see Table P for a description of each). If the number of events for a given class is higher than the number of participants, it is because some participants experienced multiple events. The single AE in the psychiatric disorders class with the preferred term, emotional stress, was associated with the participant assignment to receive an EMOT.

Table O. Serious Adverse Event (SAE) Data coded in MedDRA version 20.0

System Organ Classes	# Events	# Unique Participants
Cardiac disorders	18	8
Ear and labyrinth disorders	1	1
Gastrointestinal disorders	2	1
General disorders and administration site conditions	6	5
Hepatobiliary disorders	2	1
Infections and infestations	12	9
Injury, poisoning and procedural complications	2	2
Investigations	1	1
Metabolism and nutrition disorders	4	4
Musculoskeletal and connective tissue disorders	4	4
Neoplasms benign, malignant, and unspecified (including cysts and polyps)	4	3
Nervous system disorders	8	6
Psychiatric disorders	27	20
Renal and urinary disorders	1	1
Respiratory, thoracic and mediastinal disorders	4	4
Social circumstances	1	1
Surgical and medical procedures	11	11
Vascular disorders	1	1
Total	**109**	**57**

Table P. Adverse Event (AE) Data Coded in MedDRA version 20.0

System Organ Classes	Description	# Events	# Unique Participants
Immune system disorders	Participant had pre-existing allergy; exacerbated by study dog.	1	1
Infections and infestation	Tick found on participant's body.	1	1
Injury, poisoning and procedural complications	Participant had a history of degenerative joint disease and previous shoulder injury; dog pulling on leash exacerbated shoulder injury and cause a limb injury (ankle). On another occasion, while playing with study dog, the participant fell. Participant and partner, each sustained minor injury, described as skin contact by teeth but no puncture (Level 2 out of 6 on Dunbar Dog Bite Scale). No treatment required.	5	2
Psychiatric disorders	Participant was distressed about receiving an EMOT.	1	1
Total		**8**	**5**

B. Characteristics at baseline

A summary of the demographic characteristics for all participants paired with a study dog by VA study site is detailed in Appendix B – Part A: Table WW. Participant characteristics by treatment group (EMOT versus SERV) are shown in Table Q. Participants paired with a dog were on average 50.6 years old (SD=13.6; range 22-79), mostly male (80.1%), white (66.3%), and non-Hispanic (91.2%). The only significant baseline demographics difference found was in part-time volunteer status; participants in the EMOT group (n=11) volunteered more than those in the SERV group (n=4).

Table Q. Demographics for Participants Paired with a Study Dog, by Treatment Group

		EMOT (n= 84)	SERV (n= 97)	Total (n=181)
Age (years)	n	84	97	181
	Mean (SD)	49.2 (13.25)	51.8 (13.87)	50.6 (13.61)
	Median	49.0	53.0	51.0
	Min, Max	22, 73	24, 79	22, 79
Gender	n	84	97	181
Male	n (%)	70 (83.3)	75 (77.3)	145 (80.1)
Female	n (%)	14 (16.7)	22 (22.7)	36 (19.9)
Race	n	84	97	181
American Indian or Alaskan Native	n (%)	2 (2.4)	1 (1.0)	3 (1.7)
Asian	n (%)	2 (2.4)	0 (0.0)	2 (1.1)
Black, or African-American	n (%)	12 (14.3)	10 (10.3)	22 (12.2)

Native Hawaiian or Pacific Islander	n (%)	0 (0.0)	1 (1.0)	1 (0.6)
White	n (%)	52 (61.9)	68 (70.1)	120 (66.3)
Unknown	n (%)	0 (0.0)	1 (1.0)	1 (0.6)
Other	n (%)	1 (1.2)	0 (0.0)	1 (0.6)
Multiple Races	n (%)	15 (17.9)	16 (16.5)	31 (17.1)
Ethnicity	n	84	97	181
Hispanic	n (%)	8 (9.5)	4 (4.1)	12 (6.6)
Not Hispanic	n (%)	74 (88.1)	91 (93.8)	165 (91.2)
Unknown	n (%)	2 (2.4)	2 (2.1)	4 (2.2)
Marital Status	n	84	97	181
Married	n (%)	35 (41.7)	34 (35.1)	69 (38.1)
Co-habitating	n (%)	5 (6.0)	4 (4.1)	9 (5.0)
Widowed	n (%)	3 (3.6)	2 (2.1)	5 (2.8)
Never Married	n (%)	11 (13.1)	13 (13.4)	24 (13.3)
Divorced	n (%)	27 (32.1)	38 (39.2)	65 (35.9)
Separated	n (%)	3 (3.6)	6 (6.2)	9 (5.0)
Education Level	n	84	97	181
< High School Diploma	n (%)	2 (2.4)	1 (1.0)	3 (1.7)
High School Diploma/GED	n (%)	16 (19.0)	14 (14.4)	30 (16.6)
Some College Credit	n (%)	37 (44.0)	35 (36.1)	72 (39.8)
Associate Degree	n (%)	9 (10.7)	22 (22.7)	31 (17.1)
Bachelor's Degree	n (%)	11 (13.1)	12 (12.4)	23 (12.7)
Master's Degree	n (%)	7 (8.3)	12 (12.4)	19 (10.5)
Ph.D. or Professional Degree	n (%)	2 (2.4)	1 (1.0)	3 (1.7)
Income Level	n	84	97	181
< $10,000	n (%)	3 (3.6)	7 (7.2)	10 (5.5)
$10,001 - $20,000	n (%)	10 (11.9)	15 (15.5)	25 (13.8)
$20,001 - $30,000	n (%)	11 (13.1)	14 (14.4)	25 (13.8)
$30,001 - $40,000	n (%)	15 (17.9)	14 (14.4)	29 (16.0)
$40,001 - $50,000	n (%)	15 (17.9)	14 (14.4)	29 (16.0)
$50,001 - $60,000	n (%)	13 (15.5)	15 (15.5)	28 (15.5)
$60,001 - $70,000	n (%)	8 (9.5)	11 (11.3)	19 (10.5)
> $70,001	n (%)	9 (10.7)	6 (6.2)	15 (8.3)
Missing	n (%)	0 (0.0)	1 (1.0)	1 (0.6)
Walk Outside	n	84	97	181
Never	n (%)	8 (9.5)	6 (6.2)	14 (7.7)
One or time times a week	n (%)	20 (23.8)	20 (20.6)	40 (22.1)
At least once a day	n (%)	37 (44.0)	49 (50.5)	86 (47.5)
More than once a day	n (%)	17 (20.2)	22 (22.7)	39 (21.5)
Missing	n (%)	2 (2.4)	0 (0.0)	2 (1.1)
Served Outside US	n	84	97	181
No	n (%)	6 (7.1)	8 (8.2)	14 (7.7)
Yes	n (%)	78 (92.9)	89 (91.8)	167 (92.3)
Served in Combat Area	n	84	97	181
No	n (%)	17 (20.2)	30 (30.9)	47 (26.0)
Yes	n (%)	67 (79.8)	67 (69.1)	134 (74.0)
Hearing Impairment	n	84	97	181
No	n (%)	50 (59.5)	45 (46.4)	95 (52.5)
Yes	n (%)	34 (40.5)	51 (52.6)	85 (47.0)

Missing	n (%)	0 (0.0)	1 (1.0)	1 (0.6)
Visual Impairment	n	84	97	181
No	n (%)	69 (82.1)	80 (82.5)	149 (82.3)
Yes	n (%)	15 (17.9)	17 (17.5)	32 (17.7)
Mobility Impairment	n	84	97	181
No	n (%)	52 (61.9)	64 (66.0)	116 (64.1)
Yes	n (%)	32 (38.1)	32 (33.0)	64 (35.4)
Missing	n (%)	0 (0.0)	1 (1.0)	1 (0.6)
Alternative Therapy	n	84	97	181
No	n (%)	52 (61.9)	61 (62.9)	113 (62.4)
Yes	n (%)	32 (38.1)	36 (37.1)	68 (37.6)
Branch of Military	n	84	97	181
Army	n (%)	44 (52.4)	52 (53.6)	96 (53.0)
Navy	n (%)	15 (17.9)	14 (14.4)	29 (16.0)
Air Force	n (%)	7 (8.3)	10 (10.3)	17 (9.4)
Marines	n (%)	18 (21.4)	23 (23.7)	41 (22.7)
Coast Guard	n (%)	0 (0.0)	2 (2.1)	2 (1.1)
Merchant Marines	n (%)	0 (0.0)	0 (0.0)	0 (0.0)
National Guard	n (%)	10 (11.9)	10 (10.3)	20 (11.0)
When Served	n	84	97	181
World War I	n (%)	0 (0.0)	0 (0.0)	0 (0.0)
World War II	n (%)	0 (0.0)	0 (0.0)	0 (0.0)
Korean conflict	n (%)	0 (0.0)	1 (1.0)	1 (0.6)
Vietnam conflict	n (%)	21 (25.0)	29 (29.9)	50 (27.6)
Gulf War	n (%)	30 (35.7)	23 (23.7)	53 (29.3)
Balkans conflict	n (%)	2 (2.4)	2 (2.1)	4 (2.2)
Afghanistan conflict	n (%)	11 (13.1)	19 (19.6)	30 (16.6)
Iraq conflict	n (%)	29 (34.5)	32 (33.0)	61 (33.7)
Peace time	n (%)	13 (15.5)	25 (25.8)	38 (21.0)
Other conflict	n (%)	9 (10.7)	12 (12.4)	21 (11.6)
Work Status	n	84	97	181
Working part or full time	n (%)	25 (29.8)	26 (26.8)	51 (28.2)
Student full time	n (%)	4 (4.8)	12 (12.4)	16 (8.8)
Student part time	n (%)	4 (4.8)	1 (1.0)	5 (2.8)
Homemaker	n (%)	2 (2.4)	0 (0.0)	2 (1.1)
Retired not due to disability	n (%)	15 (17.9)	17 (17.5)	32 (17.7)
Volunteer full time	n (%)	0 (0.0)	0 (0.0)	0 (0.0)
Volunteer part time	n (%)	11 (13.1)	4 (4.1)	15 (8.3)
Disabled: unable to work due to physical disability	n (%)	29 (34.5)	31 (32.0)	60 (33.1)
Disabled: unable to work due to mental health status	n (%)	34 (40.5)	44 (45.4)	78 (43.1)
Unemployed and not seeking work	n (%)	7 (8.3)	6 (6.2)	13 (7.2)
Unemployed actively seeking work	n (%)	1 (1.2)	3 (3.1)	4 (2.2)
Other work status	n (%)	1 (1.2)	2 (2.1)	3 (1.7)

Three vendors provided dogs for the study. Most dogs were Labrador Retriever/Golden Retriever crosses, followed by Labrador Retrievers (LR), Golden Retrievers (GR), and German

Shepherds, respectively. Vendor 1 provided slightly over half of all study dogs. The distribution of dogs by vendor, breed, gender and dog type is shown in Table R.

Table R. Dog allocation by vendor, breed, gender, and type

	Labrador Ret EMOTs	Labrador Ret SERVs	LR X GR EMOTs	LR X GR SERVS	Golden Ret EMOTs	Golden Ret SERVs	German Shep EMOTs	German Shep SERVs
Vendor 1	3 F / 1 M	4F / 5 M	14 F / 19 M	24 F / 19 M		1 M		
Vendor 2	11 F / 11 M	7F / 18 M				1M	2F / 1M	
Vendor 3	8 F / 9 M	5 F / 10 M			1F	1M		
Totals	22 F / 21M	16F / 33M	14 F /19 M	24 F / 19 M	1F	3M	2F / 1M	

Vendor 1 = 90 dogs (37 EMOTs / 53 SERVs)
Vendor 2 = 51 dogs (25 EMOTs/ 26 SERVs)
Vendor 3 = 34 dogs (18 EMOTs /16 SERVs)

All individuals enrolled in the study were confirmed to have a diagnosis of PTSD based on the CAPS. CAPS PTSD severity scores at screening showed no difference between treatment groups as shown in Table S.

Table S. CAPS PTSD severity score at Screening

EMOT				SERV				Total				
N	Mean	SD	Median	N	Mean	SD	Median	N	Mean	SD	Median	Wilcoxon P-value
84	40.08	10.32	39.0	97	39.59	9.38	40.0	181	39.82	9.80	40.0	0.924

Using the MINI, the most prevalent DSM-5 psychiatric diagnosis at clinic screening visit was major depression for both the EMOT and SERV groups. No treatment group differences in the prevalence of each diagnosis at screening was found (see Table T).

Table T. Incidence of DSM-5 psychiatric diagnoses at Screening per the MINI

	EMOT (n= 84)		SERV (n= 97)		
Diagnosis	Does Not Meet Criteria n(%)	Meets Criteria n(%)	Does Not Meet Criteria n(%)	Meets Criteria n(%)	P-value
Major Depressive Episode: Current (2 weeks)	42 (50.0)	42 (50.0)	52 (53.6)	45 (46.4)	0.628
Major Depressive Episode: Past	17 (20.2)	67 (79.8)	10 (10.3)	87 (89.7)	0.061
Major Depressive Episode: Recurrent	47 (56.0)	37 (44.0)	48 (49.5)	49 (50.5)	0.385
Major Depressive Disorder: Current (2 weeks)	52 (61.9)	32 (38.1)	63 (64.9)	34 (35.1)	0.671
Major Depressive Disorder: Past	33 (39.3)	51 (60.7)	37 (38.1)	60 (61.9)	0.875
Major Depressive Disorder: Recurrent	59 (70.2)	25 (29.8)	71 (73.2)	26 (26.8)	0.659
Manic Episode: Current	84 (100.0)	0 (0.0)	96 (99.0)	1 (1.0)	>0.999
Manic Episode: Past	80 (95.2)	4 (4.8)	90 (92.8)	7 (7.2)	0.491
Hypomanic Episode: Current	84 (100.0)	0 (0.0)	97 (100.0)	0 (0.0)	---
Hypomanic Episode: Past	82 (97.6)	2 (2.4)	94 (96.9)	3 (3.1)	>0.999
Bipolar I Disorder: Current	82 (97.6)	2 (2.4)	96 (99.0)	1 (1.0)	0.598
Bipolar I Disorder: Past	83 (98.8)	1 (1.2)	93 (95.9)	4 (4.1)	0.375
Bipolar II Disorder: Current	84 (100.0)	0 (0.0)	97 (100.0)	0 (0.0)	---
Bipolar II Disorder: Past	84 (100.0)	0 (0.0)	96 (99.0)	1 (1.0)	>0.999

Bipolar Disorder NOS: Current	84 (100.0)	0 (0.0)	97 (100.0)	0 (0.0)	---
Bipolar Disorder NOS: Past	84 (100.0)	0 (0.0)	97 (100.0)	0 (0.0)	---
Panic Disorder: Current (past month)	72 (85.7)	12 (14.3)	86 (88.7)	11 (11.3)	0.553
Panic Disorder: Lifetime	64 (76.2)	20 (23.8)	76 (78.4)	21 (21.6)	0.729
Alcohol Use Disorder: Past 12 Months	80 (95.2)	4 (4.8)	93 (95.9)	4 (4.1)	>0.999
Substance Use Disorder: Past 12 Months	83 (98.8)	1 (1.2)	97 (100.0)	0 (0.0)	0.464
Psychotic Disorder: Current	84 (100.0)	0 (0.0)	97 (100.0)	0 (0.0)	---
Psychotic Disorder: Lifetime	84 (100.0)	0 (0.0)	97 (100.0)	0 (0.0)	---
Mood Disorder with Psychotic Features: Current	84 (100.0)	0 (0.0)	97 (100.0)	0 (0.0)	---
Mood Disorder with Psychotic Features: Lifetime	84 (100.0)	0 (0.0)	96 (99.0)	1 (1.0)	>0.999
Generalized Anxiety Disorder: Current (past 6 months)	78 (92.9)	6 (7.1)	90 (92.8)	7 (7.2)	0.985

C. Baseline and Clearing Assessments

Analyses evaluating the change in outcome measures between baseline and clearing for all participants (before pairing) are provided in Table U. Using the C-SSRS, an 11.6% increase ($p = 0.0017$) in suicide behavior or ideation occurred from baseline to clearing, along with worsening scores for activity limitations (WHO-DAS 2.0), physical health functioning (VR-12 PCS), PTSD symptoms (PCL-5), and anger (DAR). No change was observed for mental health functioning (VR-12 MCS), sleep (PSQI), or depression (PHQ-9).

Table U. Baseline to Clearing Comparison of outcome assessments

	Mean Change (Clearing-Baseline)	SD	P-value	Summary
WHO-DAS 2.0	6.03	15.44	<0.0001*	Worsened at Clearing by ~6.0
VR-12 PCS	-1.79	8.78	0.0078*	Worsened at Clearing by ~1.8
VR-12 MCS	0.12	9.95	0.8678	No difference
PSQI	0.22	3.38	0.1390*	No difference
PHQ-9	0.52	5.02	0.1616	No difference
PCL-5	2.02	11.92	0.0062*	Worsened at Clearing by ~2.0
DAR	1.64	11.91	0.0266*	Worsened at Clearing by ~1.6
C-SSRS SBI	37/181 (20.4%)	58/181 (32.0%)	0.0017	Increased at Clearing by ~11.6%

*Wilcoxon signed-rank test; otherwise, if no asterisk, a paired t-test or McNemar's test was used.

D. Primary Outcomes

i. WHO-DAS 2.0 (Disability)

All results presented in this section are for the per protocol (PP) dataset. In section F. Additional Models and Appendix B, results for the PPDR dataset with dog replacement data removed are also presented. For clarity, all tables include a PP or PPDR designation, where applicable. The unadjusted WHO-DAS 2.0 summary scores over time by group are displayed in Table V whereas the WHO-DAS 2.0 domain scores by group over time are shown in Appendix B – Table AAA. In both groups, WHO-DAS 2.0 scores at 18 months decreased (less disability) from

scores observed at 3 months post pairing. For the domain of "Interpersonal Interactions," the SERV intervention group had a mean change (reduction) from baseline to 18 months of -9.7 versus -3.5 for the EMOT intervention group.

After adjusting for baseline score, center, and gender, the linear mixed repeated measures model for WHO-DAS 2.0 did not support a treatment group difference. As shown in Table W, the model showed a time effect (p=0.0003) which indicates scores changed over time. There was no significant interaction between time and group. Contrasts testing for a difference in the SERV intervention versus EMOT intervention for WHO-DAS 2.0 across time and at 18 months are displayed in Table X.1. Least square means (from the adjusted model) over time are displayed in Figure X.2 and accompanying Table X.3 with 95% confidence intervals at each visit.

Table V. Unadjusted WHO-DAS 2.0 Overall Summary Score (lower score = less disability) over time by group (PP)

	EMOT						SERV					
Visits	**N**	**Mean**	**SD**	**Min**	**Max**	**Median**	**N**	**Mean**	**SD**	**Min**	**Max**	**Median**
Baseline	83	38.31	16.23	5	92	36	97	35.78	16.72	3	84	34
Cleared	84	44.01	18.09	3	91	46	97	42.06	17.19	1	75	41
Month 3	76	41.76	16.89	2	76	42.5	95	38.76	16.46	7	81	37
Month 6	73	41.70	17.62	1	95	43	94	36.73	16.33	5	81	38
Month 9	70	43.07	18.74	2	97	42.5	92	36.90	17.29	0	80	37
Month 12	68	40.79	17.36	1	90	40	90	36.76	17.23	0	80	35.5
Month 15	66	43.48	17.83	0	92	44	88	36.16	17.69	0	85	34
Month 18	65	38.05	17.79	0	73	38	88	33.43	17.38	2	86	33

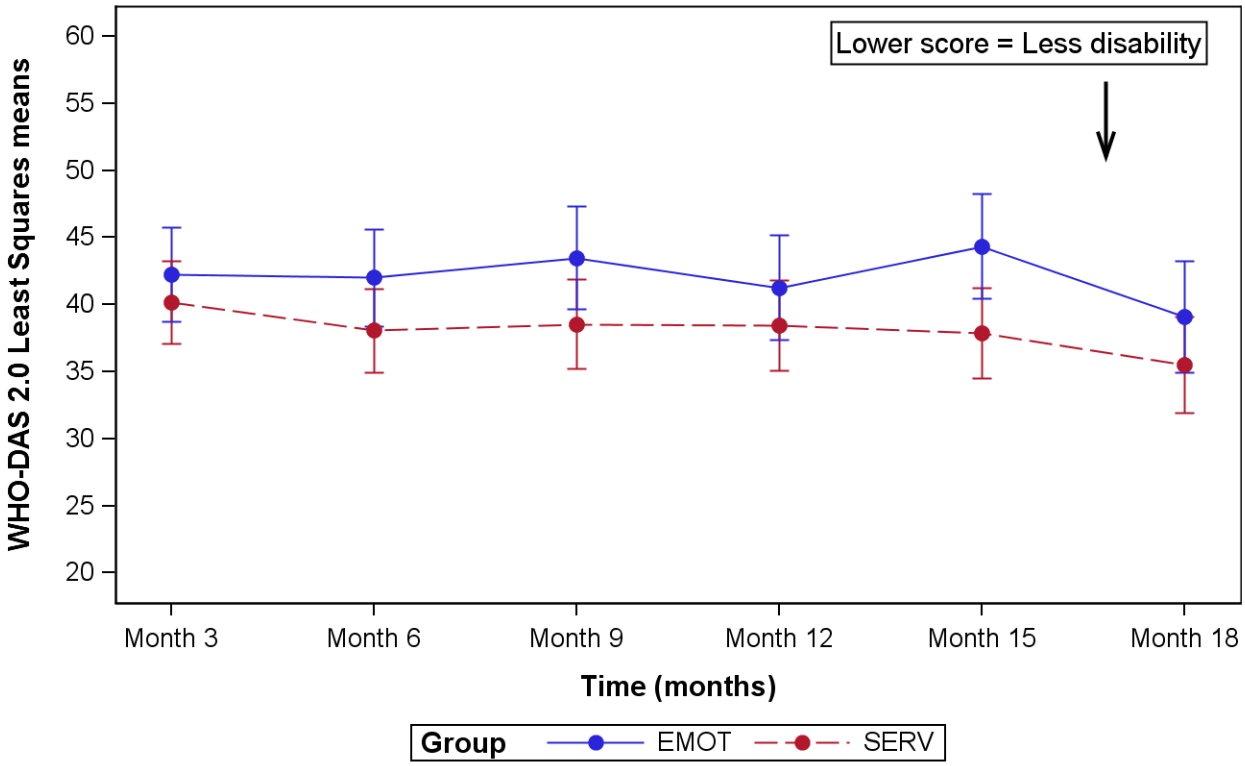
Table W. Linear Mixed Repeated Measures model results for the WHO-DAS 2.0 (PP)

		Repeated (PP)	
Outcome	**Effect**	**F statistic**	**P-value**
WHO-DAS 2.0	Baseline score	73.85	<.0001
	Gender	3.33	0.0696
	Center	6.85	0.0014
	Treatment	3.84	0.0517
	Time	4.89	0.0003
	Treatment*Time	1.43	0.2166

Table X.1. Effect of SERV Intervention vs. EMOT Intervention for WHO-DAS 2.0 (PP)

			PP			
	Outcome Measure	**Population-Model Type**	**Estimate**	**95% CI Lower**	**95% CI Upper**	**P-value**
SERV vs. EMOT over time	WHO-DAS 2.0	repeated	-3.9743	-7.9779	0.0293	0.0517
SERV vs. EMOT at 18 months	WHO-DAS 2.0	repeated	-3.6023	-8.7101	1.5054	0.1656

Figure X.2. WHO-DAS 2.0 overall summary score Least Squares Means and 95% confidence intervals over time by Treatment (lower score=improvement; PP population)



Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

Table X.3. WHO-DAS 2.0 overall summary score Least Squares Means (Adjusted) and 95% confidence intervals over time by Treatment (lower score=improvement; PP population)

	EMOT		SERV	
Time	**N**	**Adjusted Mean (95% CI)**	**N**	**Adjusted Mean (95% CI)**
3	76	42.21 (38.69, 45.74)	95	40.16 (37.09, 43.23)
6	73	42.00 (38.38, 45.61)	94	38.06 (34.92, 41.19)
9	70	43.48 (39.64, 47.32)	92	38.52 (35.19, 41.85)
12	68	41.26 (37.38, 45.15)	90	38.43 (35.07, 41.79)
15	66	44.33 (40.44, 48.23)	88	37.88 (34.51, 41.24)
18	65	39.10 (34.94, 43.26)	88	35.50 (31.89, 39.10)

Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

ii. VR-12 (Quality of Life)

The results of VR-12 PCS and MCS for PP over time by group are displayed in Table Y. No differences for physical health (PCS) were observed but some improvement in mental health (MCS) over time was observed in both groups. MCS scores were 31.11 at baseline and 39.04 at 18-months for the EMOT intervention group, and 30.68 at baseline and 40.28 at 18-months for the SERV intervention group.

Based on the linear mixed repeated measures adjusted model for quality of life, no group difference or time effect was observed for the VR-12 PCS (Table Z). For the VR-12 MCS, the model indicated a significant within-participant (i.e. time) effect after pairing ($p<0.0001$), but no treatment differences were observed. Therefore, no differences were observed for PCS (physical health), but improvements in MCS (mental health) over time were observed among both groups. Contrasts testing for a difference in the SERV intervention versus the EMOT intervention for VR-12 PCS and MCS across time and at 18 months are displayed in Table AA.1. Least square means (from the adjusted model) over time are displayed in Figures AA.2 and AA.4 accompanying Tables AA.3 and AA.5 with 95% confidence intervals at each visit.

Table Y. VR-12 PCS and MCS (higher score = better) over time by group (PP)

		EMOT						SERV					
	Visits	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**
PCS	**Baseline**	83	40.16	9.94	22.47	60.49	39.11	97	43.07	11.20	22.80	69.33	41.82
	Cleared	82	38.70	11.53	18.49	62.72	36.27	97	40.76	10.90	17.43	65.34	39.30
	Month 3	75	37.14	10.86	17.12	64.72	34.37	94	39.05	11.08	21.60	64.90	37.41
	Month 6	71	35.78	10.83	16.45	59.99	33.54	94	39.80	11.59	17.10	64.46	38.28
	Month 9	69	35.35	11.32	16.87	62.95	34.09	89	39.07	11.65	19.28	66.51	38.59
	Month 12	68	35.73	12.52	14.93	59.86	33.63	89	38.89	11.44	17.09	61.62	38.30
	Month 15	66	35.78	11.42	15.98	62.44	34.19	87	39.48	11.43	13.27	63.11	39.23
	Month 18	63	37.30	11.60	11.93	64.20	37.67	87	38.52	11.71	9.09	61.81	38.03
MCS	**Baseline**	83	31.11	10.62	13.67	59.63	29.89	97	30.68	10.37	11.71	59.33	29.79
	Cleared	82	31.14	11.04	11.18	63.80	30.59	97	30.57	10.49	7.32	63.26	30.36
	Month 3	75	35.59	10.32	12.16	61.00	35.09	94	35.81	9.07	15.00	55.97	36.12
	Month 6	71	36.71	11.30	12.27	61.85	35.89	94	35.71	8.91	17.31	55.54	35.99
	Month 9	69	34.53	10.59	12.11	60.99	33.47	89	36.39	9.92	14.27	54.65	37.51
	Month 12	68	37.32	10.66	19.54	63.84	36.06	89	36.98	10.83	14.65	60.98	38.20
	Month 15	66	36.42	10.15	19.16	60.26	35.44	87	37.72	11.40	13.46	62.93	38.88
	Month 18	63	39.04	12.35	12.37	60.26	38.78	87	40.28	9.33	19.33	56.48	41.28

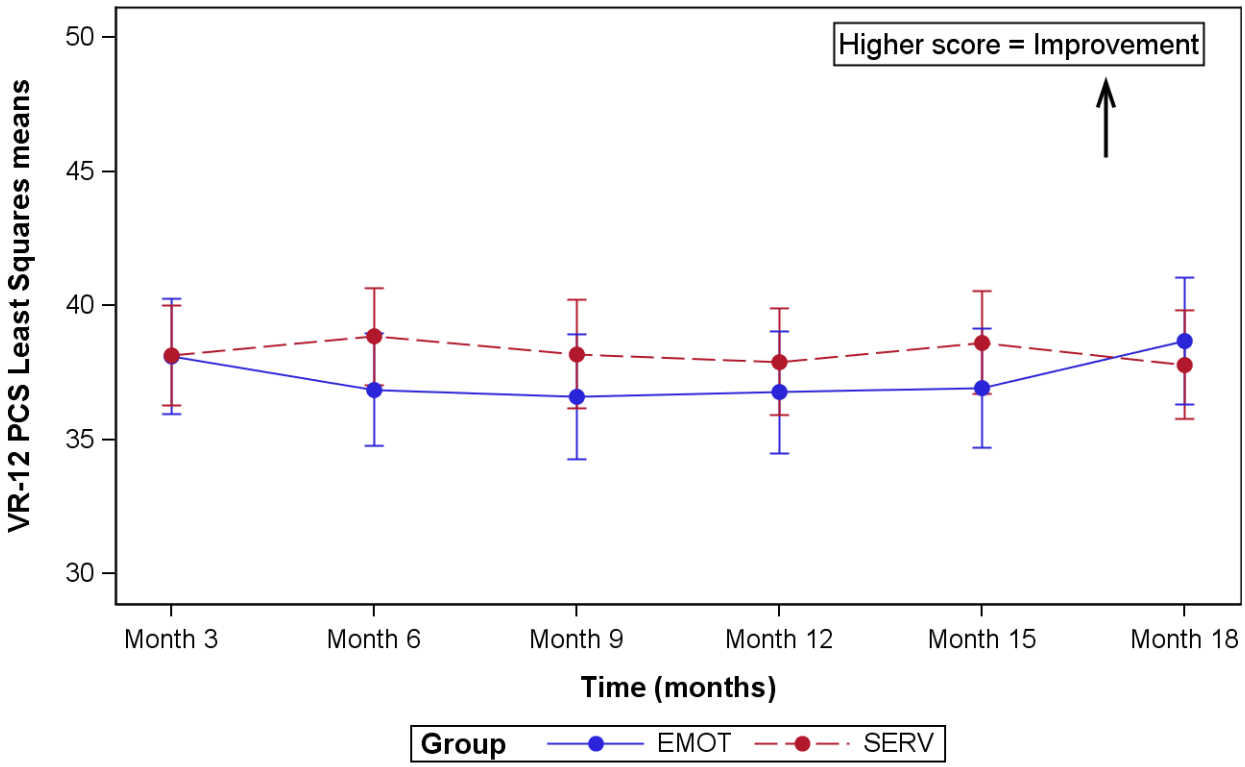
Table Z. Linear Mixed Repeated Measures model results for the VR-12 (PP)

		Repeated (PP)	
Outcome	**Effect**	**F statistic**	**P-value**
VR-12 PCS	Baseline score	163.01	<.0001
	Gender	0.10	0.7566
	Center	0.56	0.5751
	Treatment	0.65	0.4206
	Time	0.67	0.6464
	Treatment*Time	1.59	0.1661
VR-12 MCS	Baseline score	64.87	<.0001
	Gender	4.39	0.0377
	Center	3.46	0.0336
	Treatment	0.27	0.6057
	Time	5.65	<.0001
	Treatment*Time	1.73	0.1308

Table AA.1. Effect of SERV Intervention vs. EMOT Intervention for VR-12 (PP)

	Outcome Measure	Population -Model Type	PP			
			Estimate	95% CI Lower	95% CI Upper	P-value
SERV vs. EMOT over time	VR-12 PCS	repeated	0.9257	-1.3379	3.1893	0.4206
SERV vs. EMOT at 18 months	VR-12 PCS	repeated	-0.8959	-3.7781	1.9864	0.5402
SERV vs. EMOT over time	VR-12 MCS	repeated	0.5798	-1.6341	2.7938	0.6057
SERV vs. EMOT at 18 months	VR-12 MCS	repeated	1.3511	-1.7913	4.4935	0.3970

Figure AA.2. VR-12 PCS summary score Least Squares Means and 95% confidence intervals over time by Treatment (higher score=improvement; PP population)



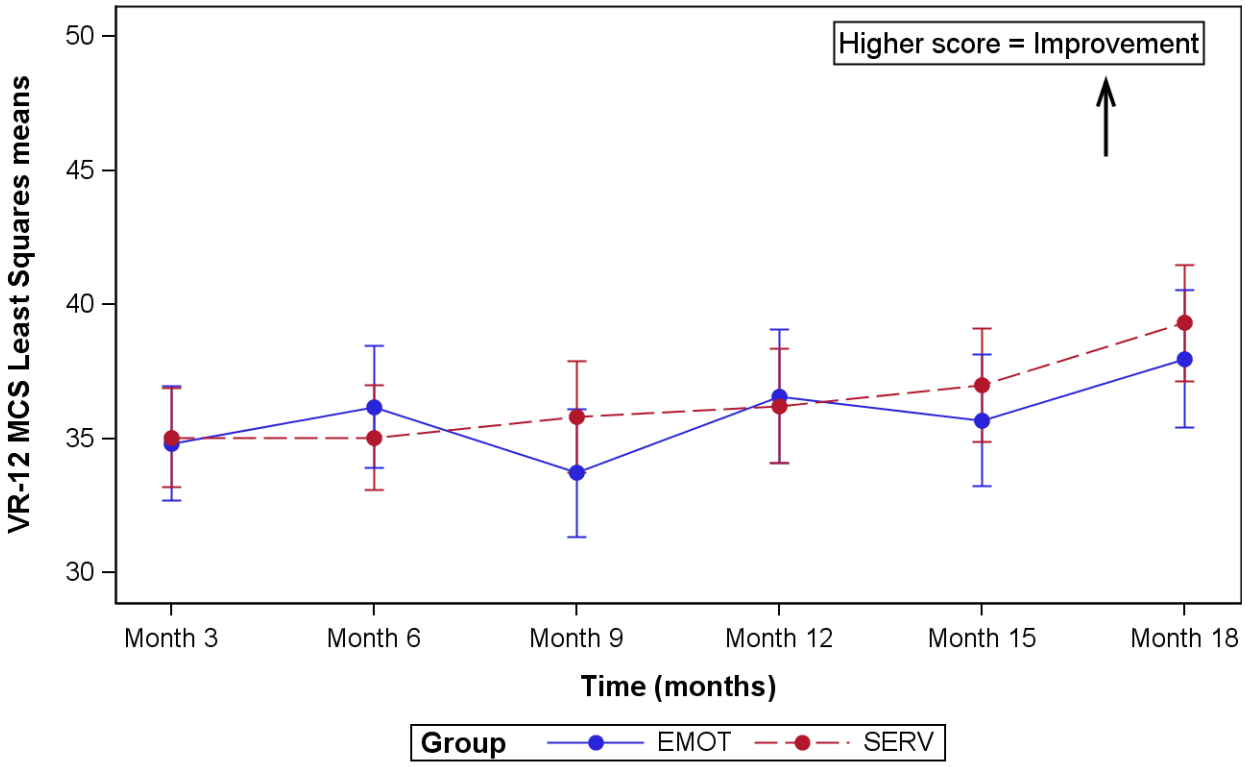
Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

Table AA.3. VR-12 PCS summary score Least Squares Means (Adjusted) and 95% confidence intervals over time by Treatment (higher score=improvement; PP population)

	EMOT		SERV	
Time	N	Adjusted Mean (95% CI)	N	Adjusted Mean (95% CI)
3	75	38.11 (35.97, 40.25)	94	38.15 (36.29, 40.02)
6	71	36.87 (34.76, 38.97)	94	38.85 (37.04, 40.67)
9	69	36.61 (34.27, 38.94)	89	38.19 (36.16, 40.22)
12	68	36.77 (34.49, 39.05)	89	37.91 (35.93, 39.88)
15	66	36.92 (34.70, 39.13)	87	38.62 (36.70, 40.53)
18	63	38.70 (36.33, 41.06)	87	37.80 (35.78, 39.82)

Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

Figure AA.4. VR-12 MCS summary score Least Squares Means and 95% confidence intervals over time by Treatment (higher score = improvement; PP population)



Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

Table AA.5. VR-12 MCS summary score Least Squares Means (Adjusted) and 95% confidence intervals over time by Treatment (higher score=improvement; PP population)

	EMOT		SERV	
Time	N	Adjusted Mean (95% CI)	N	Adjusted Mean (95% CI)
3	75	34.82 (32.69, 36.96)	94	35.04 (33.19, 36.89)
6	71	36.19 (33.91, 38.46)	94	35.04 (33.08, 37.01)
9	69	33.73 (31.34, 36.12)	89	35.82 (33.75, 37.89)
12	68	36.58 (34.10, 39.06)	89	36.22 (34.09, 38.36)
15	66	35.68 (33.22, 38.15)	87	37.00 (34.89, 39.11)
18	63	37.97 (35.42, 40.53)	87	39.32 (37.16, 41.49)

Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

This study had multiple primary outcomes (WHO-DAS, VR-12 MCS, and VR-12 PCS), but without an alpha adjustment which was a design overlook. We took this into consideration when interpreting results, which does not impact the results of the trial given no differences were observed among the primary outcomes.

E. Secondary Outcomes (including suicidality)

i. PSQI (Sleep)

Descriptive statistics for sleep quality as measured by the PSQI total score over time by group are displayed in Table BB; component scores are presented in Appendix B – Part A: Table FFF. There was a consistent separation in PSQI total scores between groups over time, as well as a decline in scores (improved sleep quality) over time in both groups. PSQI scores were 14.26 at baseline and 12.54 at 18 months for the EMOT intervention, and 13.60 at baseline and 11.74 at 18 months for the SERV intervention.

For the PSQI total score, the linear mixed repeated measures adjusted model for PSQI did not show a group difference but did indicate a significant time effect (p-value=0.0110; as evidenced by decreased scores over time (see Table CC)). Thus, an improvement in PSQI over time was observed, with no difference shown between groups. Contrasts testing for a difference in the SERV intervention versus the EMOT intervention for PSQI across time and at 18 months are displayed in Table DD.1. Least squares means (from the adjusted model) over time are displayed in Figure DD.2 and accompanying Table DD.3 with 95% confidence intervals at each visit.

Table BB. PSQI Total Score (lower score = better) over time by group (PP)

	EMOT						SERV					
Visits	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**
Baseline	84	14.26	4.09	3.00	21.00	15.00	96	13.60	3.85	2.00	20.00	14.00
Cleared	83	14.63	4.10	3.00	21.00	15.00	97	13.76	4.17	3.00	21.00	15.00
Month 3	75	13.60	4.79	1.00	20.00	15.00	95	12.51	4.24	4.00	21.00	13.00
Month 6	73	13.10	4.60	1.00	21.00	13.00	94	12.17	4.13	4.00	21.00	12.50
Month 9	69	13.29	4.59	2.00	21.00	13.00	91	12.36	4.37	3.00	21.00	13.00
Month 12	68	13.24	4.88	2.00	21.00	14.00	90	12.27	4.34	4.00	21.00	13.00
Month 15	64	12.91	4.64	1.00	20.00	13.00	88	12.02	4.50	3.00	21.00	13.00
Month 18	65	12.54	4.85	2.00	20.00	14.00	87	11.74	4.33	2.00	21.00	12.00

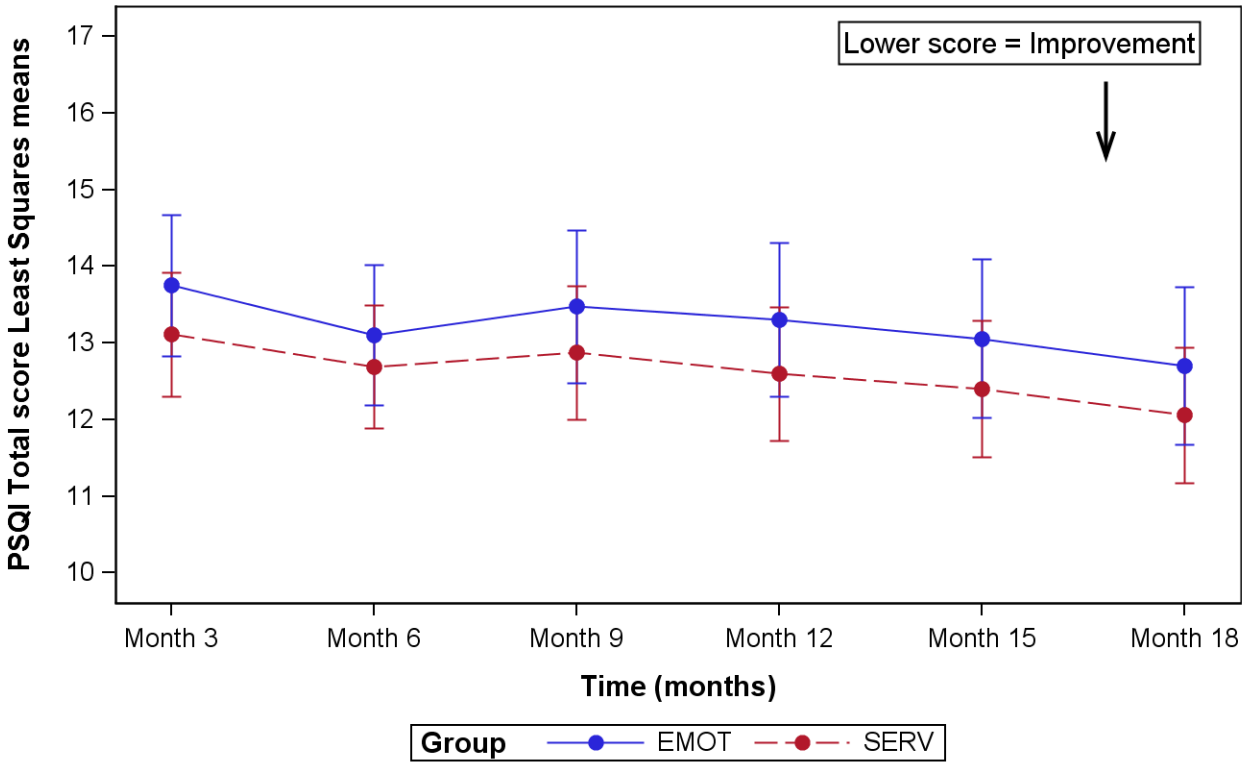
Table CC. Linear Mixed Repeated Measures model results for the PSQI (PP)

		Repeated (PP)	
Outcome	**Effect**	**F statistic**	**P-value**
PSQI	Baseline score	95.49	<.0001
	Gender	3.20	0.0755
	Center	1.91	0.1513
	Treatment	1.58	0.2104
	Time	3.08	0.0110
	Treatment*Time	0.07	0.9965

Table DD.1. Effect of SERV Intervention vs. EMOT Intervention for PSQI (PP)

	Outcome Measure	**Population-Model Type**	**PP**			
			Estimate	**95% CI Lower**	**95% CI Upper**	**P-value**
SERV vs. EMOT over time	PSQI	repeated	-0.6100	-1.5678	0.3479	0.2104
SERV vs. EMOT at 18 months	PSQI	repeated	-0.6441	-1.8980	0.6098	0.3119

Figure DD.2. PSQI total score Least Squares Means and 95% confidence intervals over time by Treatment (lower score=improvement; PP population)



Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

Table DD.3. PSQI total score Least Squares Means (Adjusted) and 95% confidence intervals over time by Treatment (lower score=improvement; PP population)

	EMOT		SERV	
Time	**N**	**Adjusted Mean (95% CI)**	**N**	**Adjusted Mean (95% CI)**
3	75	13.75 (12.83, 14.67)	95	13.11 (12.30, 13.92)
6	73	13.10 (12.19, 14.02)	94	12.69 (11.89, 13.49)
9	69	13.47 (12.48, 14.47)	91	12.87 (12.00, 13.74)
12	68	13.30 (12.30, 14.30)	90	12.59 (11.72, 13.47)
15	64	13.05 (12.02, 14.09)	88	12.40 (11.51, 13.29)
18	65	12.70 (11.68, 13.72)	87	12.06 (11.17, 12.94)

Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

ii. C-SSRS (Suicidality)

Descriptive statistics for the C-SSRS over time by group are displayed in Table EE, which includes 3 composite endpoints: suicidal ideation, suicidal behavior, and suicidal behavior or ideation (SBI). A total of 9 (5.0%) participants (5 EMOT and 4 SERV) reported suicidal behavior at any time post-pairing. As these 9 participants also reported suicidal ideation, the results for the suicidal ideation and SBI endpoints were identical. From Table EE, the rates of SBI between groups appear to overlap with some separation starting to appear during month 15 and 18. The SBI rate was 15.5% at baseline and 27.7% at 18 months for the EMOT intervention, and 24.7% at baseline and 14.8% at 18 months for SERV intervention.

The linear mixed repeated measures adjusted model for C-SSRS SBI indicated a significant time effect (p-value = 0.0441) but did not show a treatment group difference or time by treatment interaction effect (see Table FF). Therefore, changes in SBI over time were observed but without a difference between groups over time. Contrasts testing for a difference in the SERV intervention versus the EMOT intervention for SBI across time and at 18 months are displayed in Table GG.1, showing a difference between groups at 18 months. Least square means (from the adjusted model, proportions) over time are displayed in Figure GG.2 and accompanying Table GG.3 with 95% confidence intervals at each visit. Contrasts testing for a difference in the SERV group versus the EMOT group for SBI (per C-SSRS) did not show a difference between groups across time, however, it did show a difference between groups at 18 months. This is consistent with the separation we begin to see between groups after 12 months (at the Month 15 and 18 visits) from the least squares means plot. Least squares means from the linear mixed repeated measures adjusted model, reported a proportion of approximately 30% in the EMOT group versus only 14% in the SERV group at 18 months after pairing. The trend indicates a potential improved SBI among the SERV group with a longer pairing.

Table EE. C-SSRS over time by group (PP)

		EMOT (n = 84)	SERV (n = 97)	Total (n = 181)
Endpoint	**Visit**	**n (%)**	**n (%)**	**n (%)**
Suicidal Ideation	**Baseline**	13 (15.5)	24 (24.7)	37 (20.4)
	Cleared	22 (26.2)	36 (37.1)	58 (32.0)
	Month 3	22 (28.9)	33 (34.7)	55 (32.2)
	Month 6	19 (26.0)	21 (22.3)	40 (24.0)
	Month 9	19 (27.1)	22 (23.9)	41 (25.3)
	Month 12	20 (29.4)	25 (27.8)	45 (28.5)
	Month 15	21 (31.8)	20 (22.5)	41 (26.5)
	Month 18	18 (27.7)	13 (14.8)	31 (20.3)
Suicidal Behavior	**Baseline**	0 (0.0)	0 (0.0)	0 (0.0)
	Cleared	1 (1.2)	1 (1.0)	2 (1.1)
	Month 3	1 (1.3)	1 (1.1)	2 (1.2)

		EMOT (n = 84)	SERV (n = 97)	Total (n = 181)
Endpoint	**Visit**	**n (%)**	**n (%)**	**n (%)**
	Month 6	2 (2.7)	2 (2.1)	4 (2.4)
	Month 9	1 (1.4)	1 (1.1)	2 (1.2)
	Month 12	1 (1.5)	0 (0.0)	1 (0.6)
	Month 15	2 (3.0)	0 (0.0)	2 (1.3)
	Month 18	0 (0.0)	0 (0.0)	0 (0.0)
Suicidal Ideation or Behavior (SBI)	**Baseline**	13 (15.5)	24 (24.7)	37 (20.4)
	Cleared	22 (26.2)	36 (37.1)	58 (32.0)
	Month 3	22 (28.9)	33 (34.7)	55 (32.2)
	Month 6	19 (26.0)	21 (22.3)	40 (24.0)
	Month 9	19 (27.1)	22 (23.9)	41 (25.3)
	Month 12	20 (29.4)	25 (27.8)	45 (28.5)
	Month 15	21 (31.8)	20 (22.5)	41 (26.5)
	Month 18	18 (27.7)	13 (14.8)	31 (20.3)

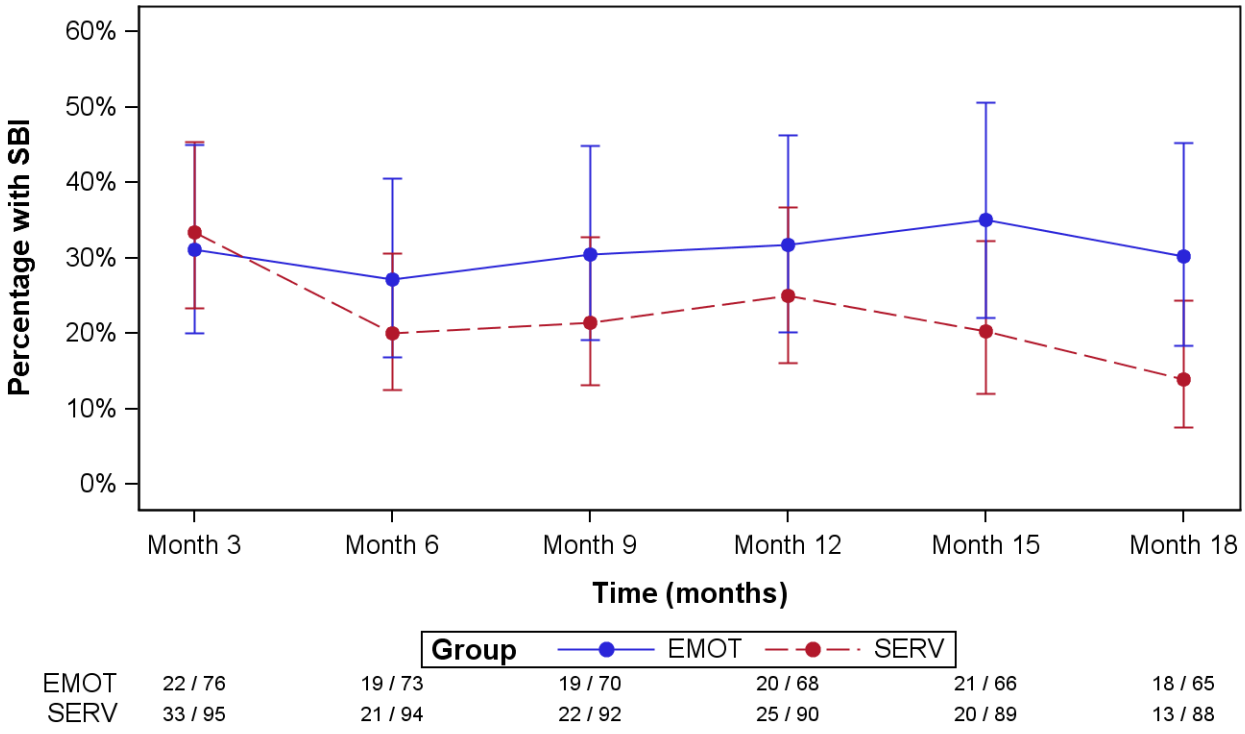
Table FF. Generalized Linear Mixed Repeated Measures model results for the C-SSRS Suicidal Behavior or Ideation (PP)

		Repeated (PP)	
Outcome	**Effect**	**F statistic**	**P-value**
C-SSRS SBI	Baseline score	13.82	0.0003
	Gender	1.63	0.2029
	Center	1.38	0.2546
	Treatment	2.03	0.1565
	Time	2.34	0.0441
	Treatment*Time	1.88	0.1008

Table GG.1. Effect of SERV Intervention vs. EMOT Intervention for C-SSRS Suicidal Behavior or Ideation (PP)

	Outcome Measure	Population-Model Type	PP			
			Estimate	95% CI Lower	95% CI Upper	P-value
SERV vs. EMOT over time	C-SSRS	repeated	-0.4730	-1.1290	0.1831	0.1565
SERV vs. EMOT at 18 months	C-SSRS	repeated	-0.9826	-1.8789	-0.08637	0.0318

Figure GG.2. C-SSRS Suicidal Behavior or Ideation (SBI) rate Least Squares Means (proportions) and 95% confidence intervals over time by Treatment (PP population)



EMOT	22 / 76	19 / 73	19 / 70	20 / 68	21 / 66	18 / 65
SERV	33 / 95	21 / 94	22 / 92	25 / 90	20 / 89	13 / 88

Note: Participants at risk for each time point: n / N where n=number of participants with SBI in the category, and N=total number of participants in the category. Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

Table GG.3. C-SSRS Suicidal Behavior or Ideation (SBI) rate Least Squares Means (Adjusted, proportions) and 95% confidence intervals over time by Treatment (PP population)

	EMOT		SERV	
Time	**n / N**	**Adjusted Proportions (95% CI)**	**n / N**	**Adjusted Proportions (95% CI)**
Month 3	22 / 76	31.15 (20.06, 44.91)	33 / 95	33.41 (23.28, 45.34)
Month 6	19 / 73	27.10 (16.84, 40.54)	21 / 94	20.03 (12.47, 30.58)
Month 9	19 / 70	30.47 (19.08, 44.90)	22 / 92	21.38 (13.20, 32.73)
Month 12	20 / 68	31.78 (20.17, 46.21)	25 / 90	24.97 (16.04, 36.70)
Month 15	21 / 66	35.03 (22.10, 50.61)	20 / 89	20.28 (11.98, 32.23)
Month 18	18 / 65	30.15 (18.39, 45.25)	13 / 88	13.91 (7.50, 24.35)

Note: Participants at risk for each time point: n / N where n=number of participants with SBI in the category, and N=total number of participants in the category. Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

iii. PCL-5 (PTSD Symptoms)

Descriptive statistics for the PCL-5 over time by group are displayed in Table HH showing a decline in scores (less symptoms of PTSD) seen in both groups. Some separation in scores between groups started at 9 months post-pairing with PCL-5 scores for the SERV intervention decreasing more than those for the EMOT intervention.

The linear mixed repeated measures adjusted model for PCL-5 indicated a significant group difference, time effect, and interaction of time and group (see Table II). Both groups were changing over time in that they experienced less symptoms of PTSD (lower PCL-5 scores), and over time the groups were changing differently. The SERV group showed a continued decrease in PCL-5 scores over time, whereas the EMOT group scores stabilized from 6 to 15 months then decreased at 18 months. Contrasts testing for a difference in the SERV intervention versus the EMOT intervention for PCL-5 across time and at 18 months are displayed in Table JJ.1, showing a difference between groups both over time and at 18 months. The model suggested approximately a 3.7 point improvement (lower score=less symptoms of PTSD) in the PCL-5 total score for SERV intervention versus EMOT intervention over time. Least square means (from the adjusted model) over time are displayed in Figure JJ.2 and accompanying Table JJ.3 with 95% confidence intervals at each visit.

Table HH. PCL-5 scores (lower score = PTSD symptom reduction) over time by group (PP)

	EMOT						SERV					
Visits	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**
Baseline	84	46.98	14.70	7.00	80.00	48.50	97	48.33	15.66	12.00	77.00	50.00
Cleared	84	49.57	14.16	13.00	78.00	50.00	97	49.85	15.14	9.00	75.00	50.00
Month 3	76	41.96	15.45	8.00	74.00	45.00	95	41.54	15.14	7.00	76.00	40.00
Month 6	73	39.66	16.43	3.00	79.00	40.00	94	39.39	14.87	10.00	79.00	37.00
Month 9	70	41.04	15.49	7.00	74.00	41.00	92	38.29	15.04	7.00	73.00	37.50
Month 12	68	40.01	17.60	2.00	79.00	42.00	90	35.48	15.39	9.00	73.00	31.50
Month 15	66	41.23	16.50	1.00	72.00	43.00	89	35.75	16.18	10.00	75.00	33.00
Month 18	65	35.25	17.00	2.00	65.00	34.00	88	31.66	14.61	9.00	72.00	29.00

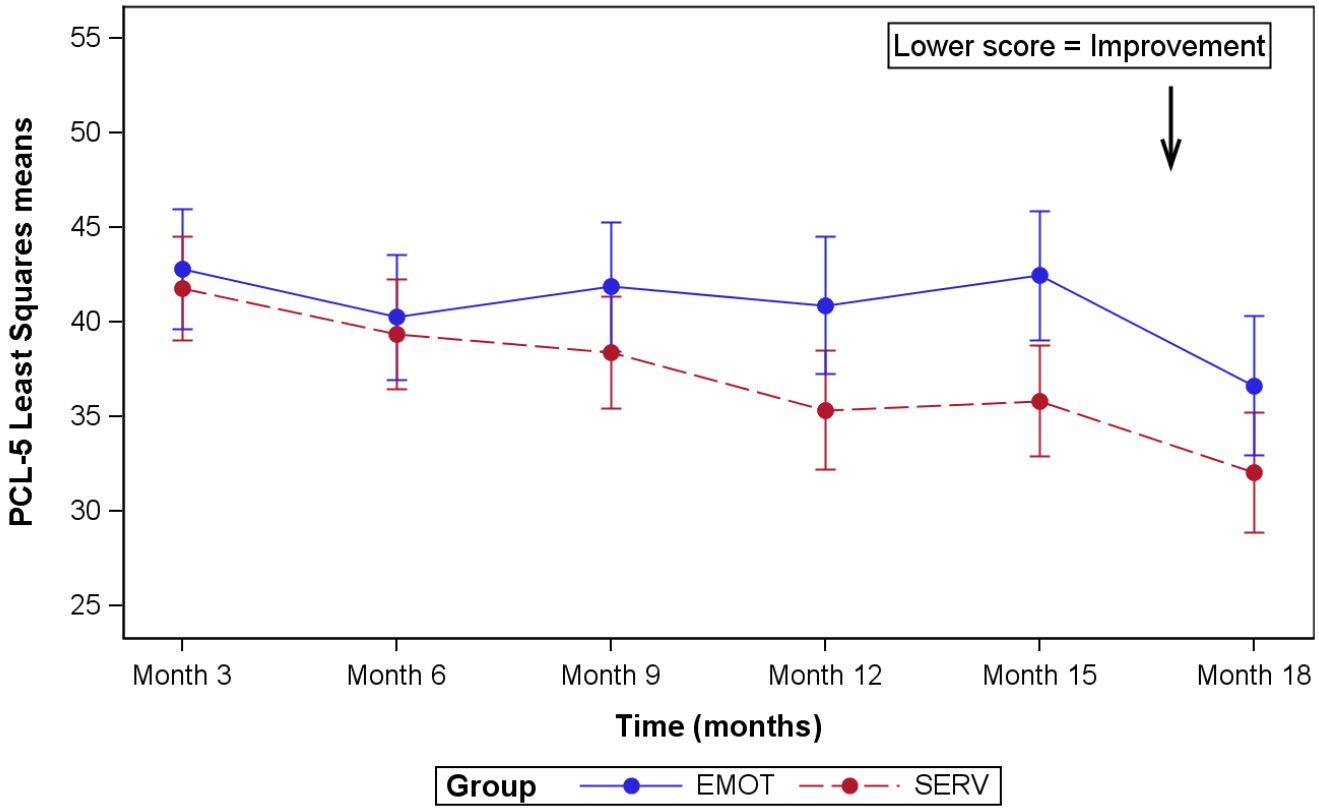
Table II. Linear Mixed Repeated Measures model results for the PCL-5 (PP)

		Repeated (PP)	
Outcome	**Effect**	**F statistic**	**P-value**
PCL-5	Baseline score	109.66	<.0001
	Gender	0.71	0.4020
	Center	3.05	0.0501
	Treatment	4.47	0.0360
	Time	13.52	<.0001
	Treatment*Time	2.52	0.0317

Table JJ.1. Effect of SERV Intervention vs. EMOT Intervention for PCL-5 (PP)

	Outcome Measure	**Population-Model Type**	**PP**			
			Estimate	**95% CI Lower**	**95% CI Upper**	**P-value**
SERV vs. EMOT over time	PCL-5	repeated	-3.6927	-7.1407	-0.2446	0.0360
SERV vs. EMOT at 18 months	PCL-5	repeated	-4.6025	-9.1027	-0.1024	0.0451

Figure JJ.2. PCL-5 score Least Squares Means and 95% confidence intervals over time by Treatment (lower score=improvement; PP population)



Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

Table JJ.3. PCL-5 score Least Squares Means (Adjusted) and 95% confidence intervals over time by Treatment (lower score=improvement; PP population)

	EMOT		SERV	
Time	**N**	**Adjusted Mean (95% CI)**	**N**	**Adjusted Mean (95% CI)**
3	76	42.80 (39.65, 45.95)	95	41.78 (39.04, 44.53)
6	73	40.26 (36.94, 43.58)	94	39.37 (36.48, 42.25)
9	70	41.89 (38.48, 45.30)	92	38.40 (35.44, 41.35)
12	68	40.89 (37.26, 44.52)	90	35.36 (32.22, 38.50)
15	66	42.46 (39.05, 45.88)	89	35.84 (32.90, 38.78)
18	65	36.65 (32.97, 40.32)	88	32.04 (28.88, 35.21)

Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

While not noted as a specific secondary outcome, PTSD symptoms were assessed at 15 months post pairing using the CAPS. The proportion of participants with PTSD at 15 months (per the CAPS) did not vary between groups (75.8% EMOT intervention versus 69.3% SERV intervention, p=0.378; see Table KK). Similarly, the CAPS total symptom severity scores also did not vary between groups either at screening (shown in Table S) or at 15 months (Table LL.1). No differences were observed between groups in changes from screening to 15 months for subscales of the CAPS (see Table LL.2).

Table KK. CAPS PTSD status at 15 months post pairing (PP)*

	EMOT		SERV		Total		
	Present	Absent	Present	Absent	Present	Absent	
Visit	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	P-value
Month 15	50 (75.8)	16 (24.2)	61 (69.3)	27 (30.7)	111 (72.1)	43 (27.9)	0.3780

*Presence of PTSD was defined as CAPS criteria A-G being satisfied

Table LL.1 CAPS total symptom severity score (PP)

	EMOT						SERV					
Visit	N	Mean	SD	Min	Max	Median	N	Mean	SD	Min	Max	Median
Screening	84	40.08	10.32	17	64	39	97	39.59	9.38	20	63	40
Month 15	66	34.97	13.40	6	66	35.5	88	32.06	11.91	7	65	33.5

Table LL2. CAPS total and subscale symptom severity score changes from screening to 15 months between groups (negative change = improvement; PP)

	EMOT						SERV						
Symptom Severity	N	Mean	SD	Min	Max	Median	N	Mean	SD	Min	Max	Median	Wilcoxon P-value
Intrusion	66	-1.45	3.40	-8.00	9.00	-2.00	88	-1.67	3.15	-8.00	7.00	-2.00	0.968
Avoidance	66	-0.83	1.72	-5.00	3.00	-1.00	88	-0.95	2.05	-7.00	4.00	-1.00	0.635
Cognition and mood	66	-2.38	5.23	-17.0	13.00	-2.50	88	-3.24	6.21	-17.0	9.00	-3.00	0.502
Arousal and reactivity	66	-1.21	3.38	-9.00	9.00	-1.00	88	-1.67	3.87	-16.0	6.00	-2.00	0.576
CAPS total	66	-5.88	10.55	-28.0	24.00	-6.50	88	-7.53	11.98	-46.0	18.00	-7.00	0.505

iv. PHQ-9 (Depression)

Descriptive statistics for the PHQ-9 over time by group are displayed in Table MM. In both groups scores declined (reduction in depression) through 6 months post pairing. The EMOT intervention group scores increased at 9 months, then stabilized until scores began to decrease again at month 18. PHQ-9 scores for the SERV intervention group steadily declined through 9 months, at which time scores stabilized until scores decreased again at 18 months. PHQ-9 scores were 13.08 at baseline and 9.43 at 18 months for EMOT intervention group, and 12.79 at baseline and 8.19 at 18 months for SERV intervention group.

For the PHQ-9, the linear mixed repeated measures adjusted model indicated a significant time effect, with a reduction in depression (lower PHQ-9 scores) observed over time ($p<0.0001$; Table NN). Despite some separation occurring after 6 months post-pairing, this difference was not great enough for models to show a significant difference by treatment assignment. In

summary, there was a significant time effect, but no treatment group difference or time by group interaction. Contrast testing for difference in the SERV intervention versus the EMOT intervention for PHQ-9 across time and at 18 months are displayed in Table OO.1. Least square means (from the adjusted model) over time are displayed in Figure OO.2 and accompanying Table OO.3 with 95% confidence intervals at each visit.

Table MM. PHQ-9 scores (lower score = better) over time by group (PP)

	EMOT						SERV					
Visits	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**
Baseline	84	13.08	5.94	0.00	25.00	13.00	97	12.79	5.85	0.00	25.00	12.00
Cleared	84	13.57	6.14	0.00	25.00	14.00	97	13.35	5.44	2.00	26.00	13.00
Month 3	76	11.46	6.05	0.00	27.00	11.00	95	10.95	5.47	0.00	24.00	11.00
Month 6	73	10.55	6.03	0.00	26.00	9.00	94	10.03	5.07	0.00	23.00	9.00
Month 9	70	11.53	6.18	0.00	25.00	11.00	92	9.52	4.80	0.00	23.00	9.00
Month 12	68	11.03	6.31	0.00	23.00	10.50	90	9.97	5.65	0.00	22.00	9.00
Month 15	66	11.47	6.20	0.00	25.00	11.00	88	9.67	5.79	0.00	24.00	9.00
Month 18	65	9.43	6.24	0.00	25.00	9.00	88	8.19	4.45	0.00	21.00	8.00

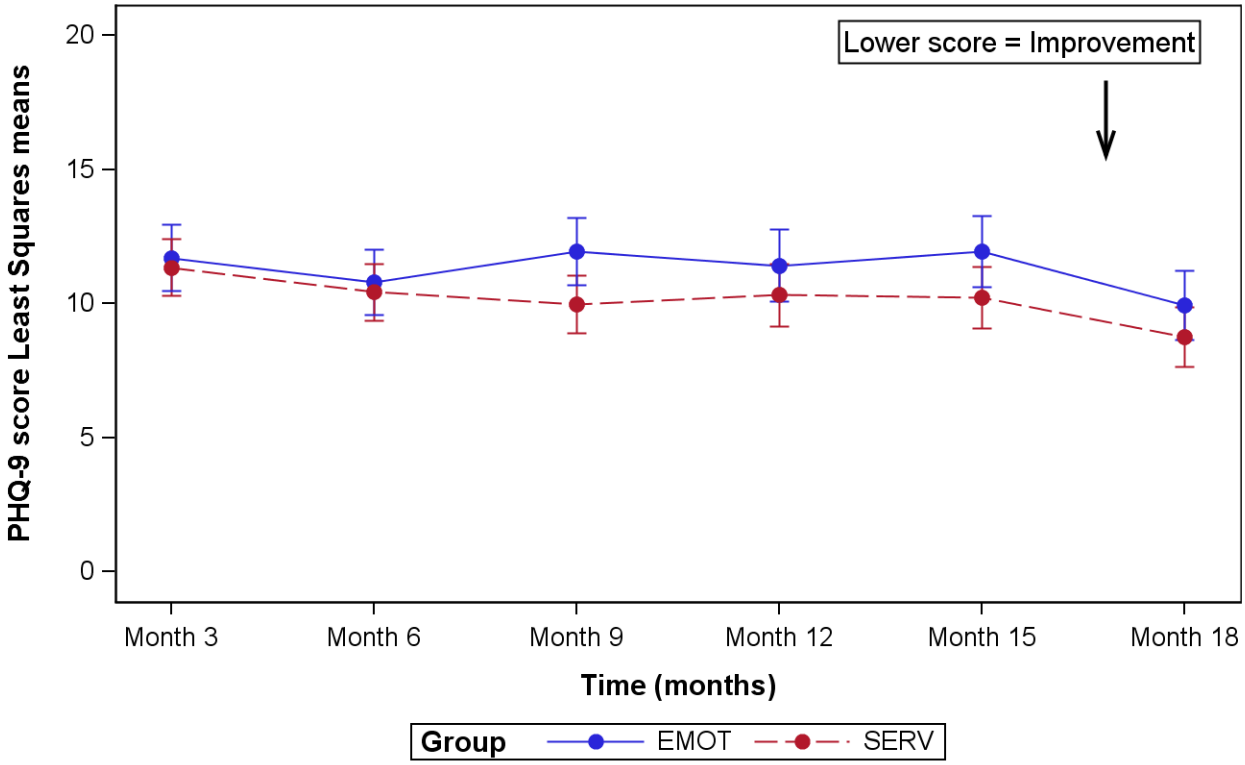
Table NN. Linear Mixed Repeated Measures model results for the PHQ-9 (PP)

		Repeated	
Outcome	**Effect**	**F statistic**	**P-value**
PHQ-9	Baseline score	69.81	<.0001
	Gender	3.13	0.0786
	Center	5.53	0.0047
	Treatment	3.13	0.0790
	Time	8.14	<.0001
	Treatment*Time	1.74	0.1280

Table OO.1. Effect of SERV Intervention vs. EMOT Intervention for PHQ-9 (PP)

			PP			
	Outcome Measure	**Population-Model Type**	**Estimate**	**95% CI Lower**	**95% CI Upper**	**P-value**
SERV vs. EMOT over time	PHQ-9	repeated	-1.1206	-2.3722	0.1311	0.0790
SERV vs. EMOT at 18 months	PHQ-9	repeated	-1.1930	-2.7751	0.3891	0.1384

Figure OO.2. PHQ-9 score Least Squares Means and 95% confidence intervals over time by Treatment (lower score=improvement; PP population)



Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

Table OO.3. PHQ-9 score Least Squares Means (Adjusted) and 95% confidence intervals over time by Treatment (lower score=improvement; PP population)

	EMOT		SERV	
Time	**N**	**Adjusted Mean (95% CI)**	**N**	**Adjusted Mean (95% CI)**
3	76	11.70 (10.47, 12.93)	95	11.35 (10.28, 12.42)
6	73	10.79 (9.57, 12.01)	94	10.42 (9.36, 11.48)
9	70	11.94 (10.70, 13.18)	92	9.97 (8.89, 11.04)
12	68	11.41 (10.07, 12.75)	90	10.31 (9.15, 11.47)
15	66	11.95 (10.62, 13.28)	88	10.21 (9.06, 11.35)
18	65	9.94 (8.64, 11.24)	88	8.75 (7.63, 9.87)

Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

v. DAR (Anger)

Descriptive statistics for the DAR for PP over time by group are displayed in Table PP. Scores declined among both groups with some separation starting after 6 months post-pairing where DAR scores for the SERV intervention group continued to decline (less symptoms of anger) but the EMOT intervention group's scores did not continue to decline. DAR scores were 23.82 at baseline and 20.15 at 18 months for the EMOT intervention, and 21.85 at baseline and 15.90 at 18 months for the SERV intervention.

The linear mixed repeated measures adjusted model for DAR indicated a significant time effect (p = 0.0005) as shown Table QQ. Both groups were changing over time in that they experienced less symptoms of anger (lower DAR scores). After 6 months post-pairing, participants in the SERV intervention group continued to have less symptoms of anger while the EMOT intervention group experienced an increase at 9 months then continued to decrease. Despite this, there were no significant differences between treatment groups. Contrast testing for a difference in the SERV intervention versus the EMOT intervention for DAR across time and at 18 months are displayed in Table RR.1. Least square means (from the adjusted model) over time are displayed in Figure RR.2 and accompanying Table RR.3 with 95% confidence intervals at each visit.

Table PP. DAR scores (lower score = better) over time by group (PP)

	EMOT						SERV					
Visits	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**
Baseline	84	23.82	14.64	0.00	54.00	22.50	97	21.85	15.07	0.00	56.00	20.00
Cleared	84	24.99	15.27	0.00	54.00	22.50	97	23.89	15.21	0.00	52.00	25.00
Month 3	76	23.21	15.87	0.00	54.00	21.00	95	22.14	14.28	0.00	52.00	22.00
Month 6	73	21.05	16.32	0.00	56.00	17.00	94	20.35	13.75	0.00	56.00	17.00
Month 9	70	23.97	16.16	0.00	56.00	23.00	92	19.52	13.22	0.00	53.00	18.50
Month 12	68	22.97	15.57	0.00	56.00	23.50	90	18.58	14.75	0.00	56.00	15.00
Month 15	66	22.32	16.91	0.00	53.00	19.00	89	17.47	14.24	0.00	56.00	15.00
Month 18	65	20.15	16.63	0.00	55.00	17.00	88	15.90	14.37	0.00	56.00	11.00

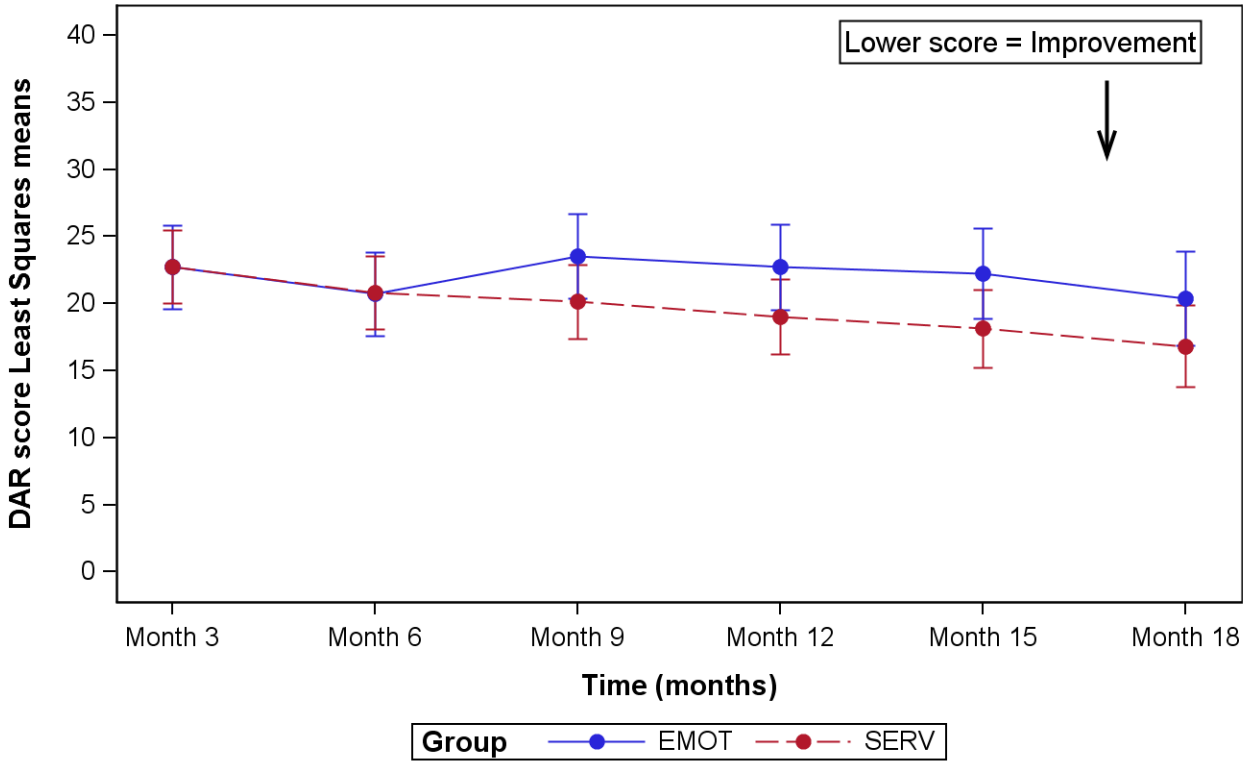
Table QQ. Linear Mixed Repeated Measures model results for the DAR (PP)

		Repeated	
Outcome	**Effect**	**F statistic**	**P-value**
DAR	Baseline score	91.55	<.0001
	Gender	0.41	0.5213
	Center	6.78	0.0015
	Treatment	2.04	0.1552
	Time	4.75	0.0005
	Treatment*Time	2.08	0.0712

Table RR.1. Effect of SERV Intervention vs. EMOT Intervention for DAR (PP)

			PP			
	Outcome Measure	**Population-Model Type**	**Estimate**	**95% CI Lower**	**95% CI Upper**	**P-value**
SERV vs. EMOT over time	DAR	repeated	-2.4380	-5.8089	0.9329	0.1552
SERV vs. EMOT at 18 months	DAR	repeated	-3.5631	-7.8772	0.7510	0.1048

Figure RR.2. DAR score Least Squares Means and 95% confidence intervals over time by Treatment (lower score=improvement; PP population)



Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

Table RR.3. DAR score Least Squares Means (Adjusted) and 95% confidence intervals over time by Treatment (lower score=improvement; PP population)

	EMOT		SERV	
Time	**N**	**Adjusted Mean (95% CI)**	**N**	**Adjusted Mean (95% CI)**
3	76	22.71 (19.61, 25.80)	95	22.74 (20.02, 25.45)
6	73	20.71 (17.61, 23.80)	94	20.79 (18.09, 23.50)
9	70	23.53 (20.37, 26.69)	92	20.13 (17.38, 22.89)
12	68	22.71 (19.50, 25.92)	90	19.02 (16.23, 21.80)
15	66	22.23 (18.88, 25.57)	89	18.13 (15.23, 21.03)
18	65	20.38 (16.85, 23.91)	88	16.81 (13.76, 19.87)

Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

F. Additional Models

The linear mixed repeated measures adjusted model was the preferred model because it used the whole per protocol dataset. For thoroughness, other models were examined, including random intercept for the PP dataset as well as the linear mixed repeated measures and random intercept models for the PPDR dataset. Other exploratory analyses were also performed.

i. PP versus PPDR models

Regardless whether the PP or PPDR datasets were used, a significant group difference was observed for the PCL-5 (PTSD symptoms) with greater improvement observed among participants paired with a SERV versus an EMOT (see Appendix B – Tables ZZ thru MMMM.5). Most models for the WHO-DAS 2.0 (disability) suggested a marginal improvement among participants paired with a SERV as compared to an EMOT. While no differences were observed for the VR-12 PCS (physical health), both groups saw improvement in the VR-12 MCS (mental health) over time as well as improvement over time for the PSQI (sleep). A significant time effect was also observed in the models for the DAR (anger), PHQ-9 (depression), and PCL-5 (PTSD symptoms) where a decline in scores was observed initially that continued beyond 6 months for the SERV intervention group. Table SS summarizes the study outcomes with significant treatment group or time effects from both the PP and PPDR datasets analyzed using repeated measures and random intercept models.

Table SS. Summary table of study outcomes by treatment group or time effects

Population: **Model:**	**PP** **Repeated**	**PP** **Random Int**	**PPDR** **Repeated**	**PPDR** **Random Int**
SERV vs. EMOT	WHO-DAS 2.0 (by~4.0) PCL-5 (by ~3.7)	WHO-DAS 2.0 (by ~4.0) PCL-5 (by ~3.6)	WHO-DAS 2.0 (by ~4.4) PCL-5 (by ~4.0)	WHO-DAS 2.0 (by ~4.4) PCL-5 (by ~3.9)
Time Effect	WHO-DAS 2.0 PCS MCS PSQI C-SSRS SBI PCL-5 PHQ-9 DAR	WHO-DAS 2.0 PCS MCS PSQI C-SSRS SBI PCL-5 PHQ-9 DAR	WHO-DAS 2.0 PCS MCS PSQI C-SSRS SBI PCL-5 PHQ-9 DAR	WHO-DAS 2.0 PCS MCS PSQI C-SSRS SBI PCL-5 PHQ-9 DAR

Observations for PP:
WHO-DAS 2.0: no significant treatment effect in the PP repeated measures model; both groups improved over time; improvement of 0.3 EMOT group and 2.4 SERV group at 18 months from baseline
PCS: no treatment group or time effects found
MCS: both groups improved over time; improvement of 7.9 EMOT group and 9.6 SERV group at 18 months from baseline
PSQI: both groups improved over time; improvement of 1.7 EMOT group and 1.9 SERV group at 18 months from baseline
C-SSRS : increase of 12.2% in SBI for EMOT group and decrease of 9.9% for SERV group at 18 months from baseline
PCL-5: a decline in scores for both groups until after 6 months where SERV group continued to decline and some separation was observed; improvement of 11.7 EMOT group and 16.7 SERV group at 18 months from baseline
PHQ-9: a decline in scores for both groups until after 6 months where SERV group continued to decline; improvement of 3.7 EMOT group and 4.6 SERV group at 18 months from baseline
DAR: a decline in scores for both groups until after 6 months where SERV group continued to decline; improvement of 3.7 EMOT group and 6.0 SERV group at 18 months from baseline

ii. Other models

Adjusted treatment effects (PP). At the completion of the study, Veterans with a SERV had significantly less PTSD symptoms as measured by the PCL-5 than Veterans with an EMOT (adjusted repeated measures treatment effect p=0.0360). Specifically, models for PP showed an improvement of approximately 3.7 points in the PCL-5 for the SERV intervention group versus the EMOT intervention group. Although the adjusted random intercept treatment model (p=0.0462) for WHO-DAS 2.0 using the PP dataset showed significantly greater improvement in disability limitations for Veterans paired with a SERV versus an EMOT (see Appendix B – Part A Table BBB), the adjusted repeated measures model (p=0.0517) did not support this finding (see Table S). Based on the PP adjusted repeated measures model, no group differences between the SERV intervention group and EMOT intervention group were observed for the VR-12 PCS (physical health) and MCS (mental health), PSQI (sleep), C-SSRS (suicidality), PHQ-9 (depression), and DAR (anger).

Adjusted time effects (PP). Improvements in scores over time from baseline to study completion (i.e. significant time effects) were observed for most study outcomes. For the PCL-5, significant improvement in PTSD symptoms was seen from baseline until the end of the study (adjusted time effect p <0.0001). In Table S, a time effect was also observed for the WHO-DAS 2.0 ([disability] adjusted repeated measures time effect p= 0.0003). Improvements in scores over time from baseline to study completion (i.e. significant time effects) were observed for the MCS ([mental health] adjusted time effect p <0.0001) and were also observed for the PSQI ([depression] adjusted repeated measures p=0.0110). No significant time effect was seen for the PCS (physical health). A significant time effect was also seen for the C-SSRS (adjusted repeated measures time effect p=0.0441) with a decreasing rate of SBI after 12 months post-pairing for the SERV intervention group that was not observed for EMOT intervention group. For both the PHQ-9 (depression) and the DAR (anger), a significant time effect was observed (PHQ-9 adjusted repeated measures time effect p <0.0001; DAR adjusted repeated measures time effect p=0.0005). Both the SERV and EMOT intervention groups improved steadily until 6 months post-pairing when the SERV intervention group continued improving while the EMOT intervention group did not until after 15 months.

Baseline to 18 months findings within each treatment group (PP). The main goal of the study was to examine the impact of pairing with SERVs compared to EMOTs on Veterans in the treatment of PTSD. The statistical analysis plan was designed and powered to address this goal. Besides determining if the SERV intervention was more beneficial than the EMOT intervention in mitigating disability and enhancing quality of life, it was important to determine the following:

- In comparison to baseline, did participants who received a SERV show improvement after pairing?

- In comparison to baseline, did participants who received an EMOT show improvement after pairing?

Therefore, post-hoc exploratory analyses that were not part of the original statistical analysis plan were performed to answer these questions.

Unadjusted score changes for SERV group from baseline to month 18. When comparing unadjusted change scores from baseline to 18 months within group, participants paired with a SERV demonstrated significant improvements at Month 18 in mental health, sleep, PTSD symptoms, depression, and anger reactions, but showed significant worsening of physical health (see Table TT). While there was a small positive change for disability (WHO-DAS 2.0) in the SERV intervention group, the improvement at Month 18 was not statistically significant. The rate of suicidality decreased from baseline (22.7%) to Month 18 (14.8%) in participants paired with a SERV, but that improvement was not statistically significant (see Table UU).

Unadjusted score changes for EMOT group from baseline to month 18. Similar to the results for SERV intervention group, participants paired with an EMOT also demonstrated improvement at 18 months relative to baseline in mental health, sleep, PTSD symptoms, and depression (see Table PP). While not statistically significant, there was some improvement in anger reactions. Also, like the SERV intervention group, those in the EMOT intervention group showed significant worsening of physical health at 18 months. There was no change for the EMOT intervention group in disability at 18 months as measured by the WHO-DAS 2.0. Suicidality increased from baseline (15.4%) to month 18 (27.7%) in the participants paired with an EMOT but the change was not statistically significant (see Table UU).

Table TT. Outcome summary of the Baseline to Month 18 change in each Treatment Group (positive change=improvement) – Unadjusted analysis (PP)

Outcome	Treatment Group	n	Mean Change	95% CI	Paired t-test p-value	Interpretation
WHO-DAS 2.0	EMOT	65	0.26	-4.42 to 4.94	0.9114	No significant change
	SERV	88	2.40	-1.74 to 6.54	0.2527	No significant change
PCS	EMOT	62	-2.68	-5.01 to -0.36	0.0243	Significant worsening in physical health
	SERV	87	-4.42	-6.57 to -2.26	0.0001	Significant worsening in physical health
MCS	EMOT	62	8.74	5.70 to 11.79	<0.0001	Significant improvement in mental health
	SERV	87	9.79	7.49 to 12.09	<0.0001	Significant improvement in mental health
PSQI	EMOT	65	2.00	0.85 to 3.15	0.0009	Significant improvement in sleep
	SERV	86	2.07	1.25 to 2.89	<0.0001	Significant improvement in sleep
PCL-5	EMOT	65	12.88	8.54 to 17.22	<0.0001	Significant improvement in PTSD symptoms
	SERV	88	16.88	13.57 to 20.18	<0.0001	Significant improvement in PTSD symptoms
PHQ-9	EMOT	65	3.98	2.35 to 5.62	<0.0001	Significant improvement in depression
	SERV	88	4.58	3.35 to 5.81	<0.0001	Significant improvement in depression
DAR	EMOT	65	3.72	-0.23 to 7.67	0.0642	Improvement in anger reactions but no significant change
	SERV	88	5.61	2.15 to 9.08	0.0018	Significant improvement in anger reactions

Table UU. Baseline and Month 18 rates of Suicidal Behavior or Ideation in each Treatment Group - Unadjusted analysis (PP)

Outcome	Treatment Group	N	Baseline n (%)	Month 18 n (%)	McNemar's test p-value	Interpretation
SBI	EMOT	65	10 (15.4%)	18 (27.7%)	0.0768	Worsening in SBI but no significant change
	SERV	88	20 (22.7%)	13 (14.8%)	0.1671	Improvement in SBI but no significant change

G. Attrition and Missing Data Analyses

Differential attrition occurred before pairing and after pairing as discussed in 4.A. Enrollment, Randomization, and Pairing - *i. Withdrawals*. Attrition after pairing was of particular concern because of its potential to influence causal effects. More participants paired with an EMOT withdrew before completing the study (18 months post pairing) than participants paired with a SERV. In the EMOT group, 19 paired participants (22.6%) of 84 did not complete the study but only 9 paired participants (9.3%) of 97 in the SERV group withdrew before study completion. A description of demographic characteristics between participants that were paired but withdrew before study completion versus those that completed the study is shown in Table VV.

When looking at the baseline assessment for each outcome and comparing participants who withdrew before study completion versus those who completed the study, no differences were observed as shown in Table WW. A multivariable logistic regression model examined attrition at 18 months post pairing using baseline characteristics. This model showed no differences, and in particular, baseline WHO-DAS 2.0 (disability) was not associated with attrition (see Appendix B: Part B -Table NNNN).

Table VV. Demographics for study completers and participants terminating early (PP)

	Statistics	Completer (n=153)	Non-completer (n= 28)	Total (n=181)
Age (years)	n	153	28	181
	Mean (SD)	50.6 (13.54)	50.7 (14.20)	50.6 (13.61)
	Median	51.0	55.5	51.0
	Min, Max	22, 79	28, 71	22, 79
Gender	N	153	28	181
Male	N (%)	121 (79.1)	24 (85.7)	145 (80.1)
Female	N (%)	32 (20.9)	4 (14.3)	36 (19.9)
Race	N	153	28	81
American Indian or Alaskan Native	N (%)	3 (2.0)	0 (0.0)	3 (1.7)
Asian	N (%)	1 (0.7)	1 (3.6)	2 (1.1)
Black, or African-American	N (%)	16 (10.5)	6 (21.4)	22 (12.2)

	Statistics	Completer (n=153)	Non-completer (n= 28)	Total (n=181)
Native Hawaiian or Pacific Islander	N (%)	0 (0.0)	1 (3.6)	1 (0.6)
White	N (%)	104 (68.0)	16 (57.1)	120 (66.3)
Unknown	N (%)	1 (0.7)	0 (0.0)	1 (0.6)
Other	N (%)	1 (0.7)	0 (0.0)	1 (0.6)
Multiple Races	N (%)	27 (17.6)	4 (14.3)	31 (17.1)
Ethnicity	N	153	28	181
Hispanic	N (%)	7 (4.6)	5 (17.9)	12 (6.6)
Not Hispanic	N (%)	142 (92.8)	23 (82.1)	165 (91.2)
Unknown	N (%)	4 (2.6)	0 (0.0)	4 (2.2)
Marital Status	N	153	28	181
Married	N (%)	57 (37.3)	12 (42.9)	69 (38.1)
Co-habitating	N (%)	6 (3.9)	3 (10.7)	9 (5.0)
Widowed	N (%)	5 (3.3)	0 (0.0)	5 (2.8)
Never Married	N (%)	23 (15.0)	1 (3.6)	24 (13.3)
Divorced	N (%)	55 (35.9)	10 (35.7)	65 (35.9)
Separated	N (%)	7 (4.6)	2 (7.1)	9 (5.0)
Education Level	N	153	28	181
< High School Diploma	N (%)	3 (2.0)	0 (0.0)	3 (1.7)
High School Diploma/GED	N (%)	25 (16.3)	5 (17.9)	30 (16.6)
Some College Credit	N (%)	63 (41.2)	9 (32.1)	72 (39.8)
Associate Degree	N (%)	25 (16.3)	6 (21.4)	31 (17.1)
Bachelor’s Degree	N (%)	20 (13.1)	3 (10.7)	23 (12.7)
Master’s Degree	N (%)	14 (9.2)	5 (17.9)	19 (10.5)
Ph.D. or Professional Degree	N (%)	3 (2.0)	0 (0.0)	3 (1.7)
Income Level	N	153	28	181
< $10,000	N (%)	9 (5.9)	1 (3.6)	10 (5.5)
$10,001 - $20,000	N (%)	24 (15.7)	1 (3.6)	25 (13.8)
$20,001 - $30,000	N (%)	20 (13.1)	5 (17.9)	25 (13.8)
$30,001 - $40,000	N (%)	27 (17.6)	2 (7.1)	29 (16.0)
$40,001 - $50,000	N (%)	24 (15.7)	5 (17.9)	29 (16.0)
$50,001 - $60,000	N (%)	20 (13.1)	8 (28.6)	28 (15.5)
$60,001 - $70,000	N (%)	16 (10.5)	3 (10.7)	19 (10.5)
> $70,001	N (%)	12 (7.8)	3 (10.7)	15 (8.3)
Missing	N (%)	1 (0.7)	0 (0.0)	1 (0.6)
Walk Outside	N	153	28	181
Never	N (%)	11 (7.2)	3 (10.7)	14 (7.7)
One or time times a week	N (%)	36 (23.5)	4 (14.3)	40 (22.1)

	Statistics	Completer (n=153)	Non-completer (n= 28)	Total (n=181)
At least once a day	N (%)	74 (48.4)	12 (42.9)	86 (47.5)
More than once a day	N (%)	31 (20.3)	8 (28.6)	39 (21.5)
Missing	N (%)	1 (0.7)	1 (3.6)	2 (1.1)
Served Outside US	N	153	28	181
No	N (%)	12 (7.8)	2 (7.1)	14 (7.7)
Yes	N (%)	141 (92.2)	26 (92.9)	167 (92.3)
Served in Combat Area	N	153	28	181
No	N (%)	42 (27.5)	5 (17.9)	47 (26.0)
Yes	N (%)	111 (72.5)	23 (82.1)	134 (74.0)
Hearing Impairment	N	153	28	181
No	N (%)	79 (51.6)	16 (57.1)	95 (52.5)
Yes	N (%)	73 (47.7)	12 (42.9)	85 (47.0)
Missing	N (%)	1 (0.7)	0 (0.0)	1 (0.6)
Visual Impairment	N	153	28	181
No	N (%)	127 (83.0)	22 (78.6)	149 (82.3)
Yes	N (%)	26 (17.0)	6 (21.4)	32 (17.7)
Mobility Impairment	N	153	28	181
No	N (%)	95 (62.1)	21 (75.0)	116 (64.1)
Yes	N (%)	57 (37.3)	7 (25.0)	64 (35.4)
Missing	N (%)	1 (0.7)	0 (0.0)	1 (0.6)
Alternative Therapy	N	153	28	181
No	N (%)	95 (62.1)	18 (64.3)	113 (62.4)
Yes	N (%)	58 (37.9)	10 (35.7)	68 (37.6)
Branch of Military	n	153	28	181
Army	N (%)	82 (53.6)	14 (50.0)	96 (53.0)
Navy	N (%)	25 (16.3)	4 (14.3)	29 (16.0)
Air Force	N (%)	15 (9.8)	2 (7.1)	17 (9.4)
Marines	N (%)	32 (20.9)	9 (32.1)	41 (22.7)
Coast Guard	N (%)	2 (1.3)	0 (0.0)	2 (1.1)
Merchant Marines	N (%)	0 (0.0)	0 (0.0)	0 (0.0)
National Guard	N (%)	15 (9.8)	5 (17.9)	20 (11.0)
When Served	n	153	28	181
World War I	N (%)	0 (0.0)	0 (0.0)	0 (0.0)
World War II	N (%)	0 (0.0)	0 (0.0)	0 (0.0)
Korean conflict	N (%)	1 (0.7)	0 (0.0)	1 (0.6)
Vietnam conflict	N (%)	41 (26.8)	9 (32.1)	50 (27.6)
Gulf War	N (%)	49 (32.0)	4 (14.3)	53 (29.3)
Balkans conflict	N (%)	4 (2.6)	0 (0.0)	4 (2.2)
Afghanistan conflict	N (%)	24 (15.7)	6 (21.4)	30 (16.6)

	Statistics	Completer (n=153)	Non-completer (n= 28)	Total (n=181)
Iraq conflict	N (%)	52 (34.0)	9 (32.1)	61 (33.7)
Peace time	N (%)	30 (19.6)	8 (28.6)	38 (21.0)
Other conflict	N (%)	17 (11.1)	4 (14.3)	21 (11.6)
Work Status	n	153	28	181
Working part or full time	N (%)	41 (26.8)	10 (35.7)	51 (28.2)
Student full time	N (%)	14 (9.2)	2 (7.1)	16 (8.8)
Student part time	N (%)	2 (1.3)	3 (10.7)	5 (2.8)
Homemaker	N (%)	2 (1.3)	0 (0.0)	2 (1.1)
Retired not due to disability	N (%)	25 (16.3)	7 (25.0)	32 (17.7)
Volunteer full time	N (%)	0 (0.0)	0 (0.0)	0 (0.0)
Volunteer part time	N (%)	12 (7.8)	3 (10.7)	15 (8.3)
Disabled: unable to work due to physical disability	N (%)	52 (34.0)	8 (28.6)	60 (33.1)
Disabled: unable to work due to mental health status	N (%)	67 (43.8)	11 (39.3)	78 (43.1)
Unemployed and not seeking work	N (%)	12 (7.8)	1 (3.6)	13 (7.2)
Unemployed actively seeking work	N (%)	3 (2.0)	1 (3.6)	4 (2.2)
Other work status	N (%)	3 (2.0)	0 (0.0)	3 (1.7)

Table WW. Baseline outcome scores for study completers and participants terminating early (PP)

	Completed				Terminated				Total				
	N	Mean	SD	Median	N	Mean	SD	Median	N	Mean	SD	Median	Wilcoxon P-value
WHO-DAS 2.0	153	36.88	15.88	34.0	27	37.33	20.00	39.0	180	36.95	16.50	35.0	0.908
PCS	152	41.79	10.96	40.5	28	41.41	9.39	40.7	180	41.73	10.71	40.7	0.954
MCS	152	30.42	9.67	29.7	28	33.36	13.97	31.7	180	30.88	10.46	29.8	0.563
PSQI	152	14.09	3.88	15.0	28	12.96	4.34	13.5	180	13.91	3.97	15.0	0.172
PCL-5	153	48.36	14.54	50.0	28	44.11	18.28	45.0	181	47.70	15.20	50.0	0.283
PHQ-9	153	13.05	5.72	12.0	28	12.29	6.78	12.0	181	12.93	5.88	12.0	0.596
DAR	153	22.52	14.73	21.0	28	24.11	15.76	22.0	181	22.76	14.86	21.0	0.673

	N	%	N	%	N	%	
C-SSRS SBI	30	19.6	7	25.0	37	20.4	0.515

Reasons for dropout in the two groups suggested no evidence of missingness not occurring at random, thus multiple imputation assuming missingness at random was employed. Multiple imputation (MI) using fully conditional specification (FCS) was performed for incomplete outcome data using the MI procedure available in SAS version 9.4 to assess the impact of missing data from differential dropout on outcome results. MI by FCS was performed using available outcome

data, including complete and incomplete outcome variables, baseline assessment data, gender, and center. Imputation models included regression for continuous variables and discriminant function for binary/categorical variables, using 10 imputations. Ten replicant datasets were created where observed data were constant across the 10 datasets and missing data were imputed for each dataset. Data were pooled using the MIANALYZE procedure and analyzed using a generalized linear mixed model assuming a binomial distribution and logit link for the C-SSRS outcome and linear mixed repeated measures and random intercept models for all other outcomes. This creates unbiased estimates, assuming the differential dropout was missing at random. The results for the PP population are shown in Table XX. The results from multiple imputation using FCS for PP and PPDR (Appendix B – Part B: Table OOOO) revealed similar treatment effects to those of the linear mixed repeated measures models for all primary and secondary outcomes with the exception of the PCL-5, which was non-significant in imputed models.

Table XX. Treatment effect based on available data and imputed data (PP)

	Available data				Imputed Data			
Outcome	Estimate	Lower 95% CI	Upper 95% CI	P-value	Estimate	Lower 95% CI	Upper 95% CI	P-value
WHO-DAS 2.0	-3.6023	-8.7101	1.5054	0.1656	-3.5367	-8.6172	1.5437	0.1722
PCS	-0.8959	-3.7781	1.9864	0.5402	-0.9607	-3.9508	2.0295	0.5278
MCS	1.3511	-1.7913	4.4935	0.3970	0.7082	-2.4388	3.8552	0.6583
PSQI	-0.6441	-1.8980	0.6098	0.3119	-0.5831	-1.8168	0.6506	0.3535
PHQ-9	-1.1930	-2.7751	0.3891	0.1384	-1.2076	-2.7457	0.3305	0.1237
PCL-5	-4.6025	-9.1027	-0.1024	0.0451	-4.3499	-8.9059	0.2062	0.0613
C-SSRS	-0.9826	-1.8789	-0.0864	0.0318	-0.9008	-1.7802	-0.0213	0.0447
DAR	-3.5631	-7.8772	0.7510	0.1048	-3.5121	-7.7157	0.6915	0.1014

5. Discussion

A. Findings

A primary goal of this study was to determine if an intervention of a SERV for Veteran participants in treatment for PTSD would improve disability and quality of life relative to an intervention of an EMOT. In the final models, we were unable to reject the null hypothesis for the primary and all but one of the secondary outcomes. This lack of difference between the two interventions for disability and quality most likely speaks to the overall beneficial effects of companion dog ownership in general.

The purpose of an EMOT is to provide comfort and companionship, which may have mental health benefits as some studies have explored. A systemic review consistent with Preferred Reporting Items for Systemic Reviews and Meta-Analyses (PRISMA) methods and reporting requirements suggested that persons with mental health problems benefited from having a companion animal, mostly dogs and cats, due to the strong human-animal bond, which helped the owners to cope more effectively during times of crisis. (Brooks, et al., 2018). Ratschen, et al., 2020 conducted a cross-sectional retrospective survey of companion animal owners (69% owned dogs) regarding their relationship and interactions with their pet during the COVID-19 lockdown

period in the United Kingdom. Having a companion animal seemed to dampen the COVID-19 lockdown effects, which notably correlated with the positive effects of a smaller reduction in mental health scores and a smaller progression in loneliness scores (Ratschen, et al.,2020). Veterans with PTSD often feel isolated and EMOTs may help ease this problem. Brooks, et al. (2018) commented that persons with mental disorders credited the presence of their pets as giving them the confidence to try new experiences and interactions with other people. Similarly, some owners of SERVs for mobility and function indicated that their dogs facilitated social engagement (Fairman & Huebner., 2000; Hart, et al., 1987). Furthermore, owners of mobility SERVs and guide dogs have also cited improvement in self-confidence, calmness, and independence, and these same benefits apply to individuals who have SERVs for autism and PTSD (Walther et al., 2017). These reports suggest that people who have SERVs for physical and/or mental disabilities experienced an improvement in their quality of life. Yamamoto and Hart, 2018 acknowledge that more research is needed, but strongly suggest that both mental health service dogs and emotional support animals can improve the lives of people with mental health disorders, consistent with the findings of our study.

Using fully adjusted statistical models, analysis of the secondary outcome of PTSD symptoms using PCL-5 revealed improvements in PTSD for the SERV intervention relative to EMOT intervention. Furthermore, additional within-group analyses demonstrated improvements in both groups overtime for the primary outcomes with the exception of physical health functioning (VR-12, PCS). These results add to a growing body of evidence suggesting the potential benefits of SERV intervention on PTSD symptoms but do not discount the value of an EMOT intervention.

Equally important, the methodology of this study directly addresses gaps in the science regarding lack of power and randomized trials– gaps which have served to divide providers across theoretical constructs of PTSD therapies and tempered the scientific community's broader acceptance of SERVs for Veterans with PTSD. Critiques of past research on potential benefits of SERVs have cited several weaknesses in approach and rigor of conclusions. For example, prior studies have lacked power to detect a difference, failed to describe the intervention dose effect (e.g., type or amount of service dog training, duration of pairing, effectiveness/quality of human dog-bond), had limited PTSD outcome measures, lacked control groups, lacked randomization or other controls for bias, and/or had inconsistent or insufficiently described data collection methods (Whitworth, et al., 2019, Van Houtert, et al., 2018; Kruger & Serpell, 2010). While most of these studies have demonstrated meaningful impacts on the subject's report of PTSD symptoms, studies have generally not followed participants long enough to determine the persistence of any benefits over time. In addition, the findings can be impacted by the type of service dog training and years of experience of the trainer or organization (Bray, et al., 2019; O'Haire, 2018). The design of this study directly addresses these gaps. The study was powered to detect a difference between EMOT and SERV intervention groups across all outcomes measured, built in a minimum 3-month observation period to mitigate the effects of the absence of a true control arm, and confirmed the status of PTSD per a gold standard (CAPS-5) at two points during study. Due to the difficulty of recruiting participants to a true no-dog control arm, this study like several others including O'Haire, 2018, used an observation or waitlist period to partially compensate for this limitation. Outcome measures were specifically selected to examine a breadth of problems commonly associated with PTSD with eight data collection points over 18 months to power the time dependent models. To further reduce data variability, the design included mandatory completion of a VA developed dog knowledge and assessment course prior pairing to ensure

participants understand their responsibilities as dog owners. The design also employed well-defined contract requirements for: (1) the breeds of dogs acceptable to VA, (2) dog health and soundness, which met or exceeded those of DOD standards for military working dogs and included medical clearance by VA veterinarians (3) well-recognized standardized tests for obedience and public access training, (4) vendor provided documentation of dog training and training competency, (5) performance testing of each dog by the VA dog trainer before acceptance as a study dog, and (6) documentation of dog performance testing by the VA National Dog Trainer. In addition, two VA dog trainers at each study site served as the consistent communication channel to identify and address dog related concerns throughout the study, which eliminated post-pairing vendor influence. Furthermore, the VA dog trainers used standardized report forms to document their observations of the participant/study dog bond, dog-related behavior, SERV or EMOT teams at study completion, and SERV and EMOT training retention at 18 months post-pairing (but participant dog handling skills were not assessed). VA dog trainers worked with participants to resolve any dog-related issues that arose. As noted throughout the monograph, these and other study forms are available for viewing at https://www.research.va.gov/programs/animal_research/ptsdstudy.cfm. The extensive qualitative data collected using these forms are being analyzed and will be reported separately.

Labrador Retriever-Golden Retriever, Labrador Retrievers, Golden Retrievers, and German Shepherds were the breeds of dogs used. These breeds were chosen because of their intelligence, trainability, and good-natured temperament. These breeds are most commonly used by ADI and IGDF organizations (Walther, et al., 2017). The dogs used as service dogs and emotional support dogs were comparable in their physical characteristics and general temperament. However, informal communication with the vendors indicated EMOTS were the ones with less ability to focus on the task at hand (i.e. distracted by squirrels, apprehensive about escalators or elevators, etc.) than service dogs. All dogs accepted by VA had to be well socialized, cooperative with their handler, nonaggressive to people and other dogs, and purpose-bred rather than shelter-sourced dogs. Consequently, all participants received a good natured and well-behaved dog. The vendors interviewed the participants to obtain personality and lifestyle information. Based upon the small need for replacement dogs, the vendors did well matching dogs to the participants. Only nine participants of the 181 participants (<5%) paired with a study dog received a replacement dog. In all cases the replacement dog was the same dog type as their original dog.

As shown in Table R, for each dog breed the distribution is relatively balanced by gender and dog type, with one exception. The exception is approximately twice as many male Labrador Retriever SERVs were paired as female SERVs of this breed This difference is likely random, and may simply have been due to male Labrador Retrievers being more readily available. Obtaining physically sound dogs with the correct temperament from reputable dogs breeders, many of which are European, was a major handicap for two of the contracted vendors and directly contributed to some participants experiencing a lengthy observation period and slightly more than half of all study dogs being provided by the vendor with its own breeding program (Vendor 1). Although the military working dogs procured by the DOD are predominantly high-drive shepherds and Malinois, the vast majority of these dogs are also obtained from European breeders (Green, 2020) and are in short supply (Vargus, 2019). The Transportation Security Administration (TSA) prefers sporting dogs such as but not limited to Labrador Retrievers and Golden Retrievers for public explosive detection work because they are less threatening to people and their hunting ability is readily

applicable to detection work. TSA detection dogs are also procured from European sources because TSA's breeding program was closed in 2012; here too the demand has outpaced the supply (Leigh, 2018). Collectively, these reports make it clear that the dog supply problem associated with this study was not unique to VA.

Examining the within-group findings reveals that Veterans receiving either intervention experienced improvements in disability and quality of life measures; the main group difference was reflected in the SERV intervention favoring a reduction in PTSD symptoms using the PCL-5. Specifically, participants paired with a SERV showed a 34.5% decrease in PCL-5 from baseline to study completion compared to a 25.0% PCL decrease over the same time period for participants paired with an EMOT. At month 18, the final PCL-5 score for those participants paired with a SERV was 31.66 versus 35.25 for those paired with an EMOT. The data from this study did not necessarily demonstrate a clinically significant change from baseline. Nonetheless, examinations of the PCL-5 have indicated that a score of 31 is a clinically relevant threshold associated with probable diagnosis of PTSD, and scores below 31 represent a symptom burden that may not require clinical intervention. Because the mean PCL-5 score for SERV participants is still slightly above the cut point of 31 (31.66) we could not substantiate that the SERV group has a demonstrable clinical advantage over the EMOT group (35.25) in PCL-5 scores (Blevins, et al., 2015). A larger proportion of Veterans paired with a SERV no longer met criteria for diagnosis of PTSD by CAPS-5 at study completion, although not significantly so (27.9% for SERV vs. 24.2% for EMOT). Unsurprisingly, the self-reported measures of PTSD (PCL-5) demonstrated a more robust response than the objective measure (CAPS), findings which could reflect Veterans' overall perception of greater SERV intervention benefit on PTSD, as described in this monograph. These findings fall in line with the other self-reported measures of improvement of activity (WHO-DAS 2.0), quality of life (VR-12 MCS), depression (PHQ-9), and anger (DAR). As SERVs differ from EMOTs in both trained tasks and public access, it is not possible to determine, in the context of the current study, the relative contribution of each to the improvements in self-reported PTSD symptoms. Additionally, those Veterans in the SERV intervention received considerably more time and attention in the instruction/pairing process because of the public access rights of SERVs, and this could also have been a factor. As noted in the methods and earlier in the discussion, at month 18, participants completed a one-on-one interview during which questions about how the dog helped them were asked. Future analyses of these data may shed light on some of these remaining questions.

Several concerns about some of the tasks used in the study for mental health were expressed by some members of the service dog community, scientists, and clinicians. The first concern is that tasks like block" and "sweep" should have been disallowed by the ADA as service dog tasks. This concern is based upon a misunderstanding of the difference between "physical protection tasks", as defined in the ADA by the Department of Justice (DoJ) and "panic protection tasks", as originally defined by Froling (1998). According to the DoJ, physical protection tasks such as unprovoked aggressive growling, barking, and biting are not appropriate service dog tasks (Federal Register, 2010), a position VA strongly endorses. In contrast, the "block" and "behind" SERV tasks used in this study involve no aggression by the dog, and are tasks given as specific examples of panic protection tasks by Froling (the dog is placed between the handler and the panic trigger, e.g. a strange person). Accordingly, these tasks are not classified as ADA physical protection tasks.

The second concern is that SERV tasks or handling a SERV represent a safety behavior which can perpetuate avoidance and the false narrative that a typical public environment is not a safe place. Some of this concern is directed at the “block” and “behind” tasks (already discussed), as well as the “sweep” task. The “sweep” task was added to the standard set of mental health tasks for the current study based upon feedback from female victims of military sexual trauma in the Tampa Phase 1 study, who relied on the sweep task to mitigate anxiety upon returning to their home alone. In our version of the sweep command, the SERV hopes to find a person in anticipation of receiving a treat. The dog is not trained to display any aggression whatsoever. As such, this task also is not a physical protection task per the ADA.

Fundamentally, these concerns with mental health SERVs are based upon a conceptualization of PTSD as a disorder of fear conditioning, in which trauma-related stimuli provoke a fear response in settings where stimuli are misperceived as a threat (e.g., slamming car door invokes threat of a gun blast). In this model, extinction of fear conditioning requires exposure to feared stimuli in a safe environment. Repeated exposure to the trauma-related stimuli, absent danger, will habituate maladaptive emotional responses and ultimately extinguish the fear response. This construct is the basis of Prolonged Exposure (PE) therapy, a first-line evidence-based intervention recommended by the VA/DOD PTSD practice guidelines (Rauch, et al. 2012; VA/DOD practice guidelines, 2017). In this model, safety behaviors (e.g., presence of a SERV) which act to reduce anxiety in fearful settings can theoretically interfere with the effectiveness of exposure therapy such that the feared stimuli are only safe in the presence of the safety behavior, which further perpetuates continued avoidance or the potential for heightened anxiety in the absence of the safety behavior. Essentially, the presence of the safety behavior precludes the individual from being able to challenge the maladaptive belief that the feared, but not objectively dangerous, stimuli are hazardous in their natural environment. Concerns have been raised that the SERVs, particularly when engaging in safety-promoting trained tasks such as “block”, “behind” or “sweep”, represent a safety behavior serving to dampen fear circuitry activation, thereby allowing the Veteran to continue to avoid the needed exposure to feared stimuli. Alternately, even if habituation of their emotional response to feared stimuli occurs, it exists only in the presence of the SERV and not “in vivo”, thereby hampering the deconditioning process independent of the SERV. Some science supports the concepts of safety behaviors reducing PE effectiveness (Foa, et al., 2007; McManus, et al., 2008; Salkovskis, et al. 1999), while others have failed to show an impact (Milosevic and Radomsky, 2008; Rachman, et al., 2011). This study’s methodology allows for a closer examination of this theoretical construct.

PE therapy (like all therapies) is not effective in all patients, with an estimated 32% of individuals remaining clinically symptomatic after a full course of PE therapy (Bradley, et al., 2005). While a nearly 70% response rate is enviable, drop-out rates prior to therapy completion range from 28% in randomized controlled trials up to 50% in real world treatment scenarios (Schottenbauer, et al., 2008; Najavits, 2015; Watts, et al., 2014; Hembree, et al., 2003). Similarly, Steenkamp, et al., 2020 reported that for up to two-thirds of patients, PE and cognitive processing therapy were not effective nor readily accepted. Conceptually, individuals with high anxiety sensitivity and behavioral avoidance tend to decline exposure-based psychotherapies, but these individuals may be more willing to accept a SERV, which is consistent with a recent report recommending that more flexible, varied, and long-term evidence-informed modular or combination treatments be pursued (Steenkamp, et al., 2020). Once paired with a SERV, these

same Veterans may be amenable to engage in previously avoided social or behavioral activities, which are consistent with observations noted anecdotally by Veterans during the study.

Those paired with SERVs would be allowed to participate in a greater range and variety of activities versus those paired with EMOTs due to the public access rights of SERVs. Moreover, these observations are consistent with data illustrating the interpersonal interactions domain of the WHO-DAS 2.0 were numerically improved among participants paired with a SERV (improving by 10.2 points from baseline to study completion) versus an EMOT (improving by 2.5 points), although the lack of statistical significance does not allow for a direct interpretation to be made. In addition, the avoidance subscale scores of the CAPS-5 demonstrate no worsening of avoidance over the course of the study for Veterans paired with SERVs (see: Table LL.2). Furthermore, if avoidance were perpetuated or worsened due to the use of SERVs, we would not expect to see the reductions in PTSD symptom severity as measured by the PCL in this group. Outside of this study's findings there are also models of PE therapy that incorporate the use of SERVs (Glintborg & Hanson, 2017). As not all treatments will be available, acceptable, or effective for all Veterans, it is important to have another modality that is beneficial and welcomed by Veterans.

In summary, we find no evidence that the use of a SERV (or EMOT) worsened PTSD or avoidance behaviors in this study, nor did we find evidence that SERVs or EMOTs interfere with PTSD recovery. Given the absence of a true control group, we cannot conclude that the changes are different than would be found in a no-dog control group. But we find no evidence that any of the service dog tasks chosen for the study adversely affected Veterans in any way. However, as a limitation, the study was not designed to specifically measure the impact of the SERV intervention or the EMOT intervention on avoidance and safety behaviors, nor were validated measures of these constructs specifically included in the study design.

It is estimated that in 2017, 16.8 Veterans completed suicide daily, a rate 50% higher than the non-Veteran adult population (US Department of Veterans Affairs, 2018). Given this statistic, suicide prevention is a core mission of the Veterans Health Administration, and opportunities or interventions which may be associated with reduction in suicidal ideation are in high need. At study conclusion, in unadjusted analyses, a reduction in suicidal ideation (SI) of 14.8% was seen in participants in the SERV group as compared to a rate of 27.7% in the EMOT group. However, after full adjustment neither model showed a treatment group difference or time by treatment interaction effect. Nonetheless, contrast testing showed a difference between groups at 18 months with the SERV group having less SI than the EMOT group. A reduction in SI is encouraging but to be meaningful this improvement in SERV group would need to be sustained over a longer period of time. Each arm demonstrated a nonsignificant increase in SI prior to pairing (observation phase) followed by a nonsignificant downward trend in SI for SERV and a slight upward trend in SI with EMOT. Compared with baseline, at study end, five more individuals paired with EMOTs reported SI as opposed to nine fewer individuals paired with SERVS reporting SI. To date, we are unaware of any other studies reporting differences in SI between participants paired with SERVs vs EMOTs. While caution must be utilized in interpreting these data given lack of statistical significance, this remains an intriguing avenue of further inquiry given the ongoing elevated rate of suicide in the veteran population and the irrevocable damage associated with this ongoing loss of life. Future studies should consider whether the suggestion of reductions in SI associated with SERV intervention can be verified.

This RCT is the largest examination to date on the impact of SERV and EMOT interventions on PTSD and was adequately powered to detect differences across a multitude of clinically relevant PTSD outcomes. However, it should be noted that this study was not designed to specifically investigate the impact of SERVs on PTSD outcomes as a primary measure, nor were concurrent treatments for PTSD, including medications and/or therapy, controlled for over the course of the study. Veterans in the study continued in their mental health care treatment as usual. Notably, the next largest study (O'Haire, 2018) demonstrated similar findings. O'Haire reported data on 141 Veterans with PTSD confirmed by PCL-5 as well as independent psychiatric review, of which 66 participants were maintained on a SERV waitlist compared to 75 participants paired with a SERV primarily from animal rescue shelters. During the length of the study, both arms received usual care but those paired with a SERV received an additional 3 weeks on-site pairing/training, a pairing process consistent with our study (1-2 weeks on site). Subjects were additionally surveyed on their bonding experience with the dog related to the training type and experiences (e.g., positive re-enforcement, bond-based). O'Haire included PTSD symptoms (self-report PCL-5), health related quality of life (VR-12), depression (PHQ-9), and measures of work functioning (WPAI). They also examined resilience, psychological wellbeing, social and work functioning, and Patient Reported Outcome Measures Information System (PROMIS), whereas our study focused on disability assessments (WHO-DAS 2.0) as a primary outcome with suicide measures (CSSR), sleep (PSQI), anger (DAR), and the clinician administered PTSD scale (CAPS-5) as secondary outcomes.

The control in O'Haire's study was the waitlist while our control was an EMOT group. Unlike our study, participants were not randomized in the O'Haire study and all participants received a service dog. Analytically, both studies used repeated measures with linear mixed effects models with hierarchical modeling and determined differences in treatment over time. Key findings were generally similar. Like our study, the O'Haire trial had a range of PCL-5 improvement, including an average drop of 21.4 points in the PCL-5 (n=35) from baseline to 3-week post-pairing and an average drop of 11.5 (n=74) at an additional single follow-up point. In comparison, the O'Haire waitlist group registered no change in PCL-5 scores; 69.7 to 66.3 from baseline to a single time point during the waitlist, respectively. In contrast, our study resulted in a mean difference in PCL-5 scores between baseline and 18 months post pairing in SERV and EMOT intervention groups from 48.3 to 31.7 (drop of 16.6) and 47.0 to 35.3 (drop of 11.7), respectively. O'Haire reported a significant improvement between baseline and waitlist versus between baseline and SERV at a cross-sectional time point (17.9 versus 14.0 respectively for group difference of -4.33; P<.001). Study findings were similar regarding measures on social isolation, social activities, and interpersonal interactions. The PROMIS subscales social activities and social isolation had a group difference (waitlist vs service dog) of 5.11 and -4.41 respectively (p<.001) whereas our study showed improvements between the EMOT intervention and SERV intervention on the subscales of the interpersonal interactions and participation in society. Overall, our two studies, which were independently designed and implemented, demonstrate generally similar improvements for participants paired with a mental health SERV on PTSD symptoms as measured by PCL-5, with notably similar findings on measures of social isolation and interpersonal interactions. As noted previously, our study and O'Haire's each lacked a true no-dog control group, so the differences found cannot with certainty be ascribed to being paired with a SERV.

In addition to the SERV intervention's impact on PTSD symptoms, the team was aware that among experienced researchers working with SERVs, there was a general expectation that SERVs would have a greater impact on general functioning. However, the final models demonstrated no significant improvements for the SERV intervention relative to the EMOT intervention on the WHO-DAS 2.0 and other measures of functioning. This was somewhat unexpected given the known positive impact of SERVs on other disabilities (e.g., mobility). Lastly, given the large number of suggestive but non-significant finding of improvements in participants assigned to the SERV intervention, even longer term follow-up is warranted in future studies.

B. Limitations

Several limitations of this study deserve discussion. The fact that both groups experienced improvement may be due to the Hawthorne effect (McCambridge, et al., 2014), which is defined as uncontrolled effects related to individuals participating in a clinical trial. Initially, participants were blinded to their group assignment but because they were participating in a research study, they expected to get better. Likewise, the attention of the study team, dog trainers, and mental health clinicians, as well as social interactions with these individuals may have further contributed to this effect. Improvements in each of the groups, in the absence of a true control group, must be considered carefully. Furthermore, failure to reject the null hypothesis for the a priori primary and secondary outcomes for between group comparisons can technically be interpreted as both 'equally effective' as well as 'equally ineffective'. Nonetheless, between group differences emerged for PTSD symptom improvement for the SERV intervention.

The gold standard implementation of an RCT is best achieved under conditions where there is true clinical equipoise and under strict blinding conditions. Clinical equipoise exists when there is true disagreement among the medical community regarding the benefit of one treatment over another, and the beliefs of the investigator are not necessarily considered. It is also argued that considerations for equipoise must exist at the participant level; beliefs that are held that one treatment will be superior to another can shape the outcome (e.g., expectancy). Pertaining to the mental health professional community beliefs, arguments laid out in the introduction support some substantial evidence that dogs benefit human physiology and certain mental health states but gaps in the literature exist as to whether more highly trained dogs can specifically benefit those with PTSD. Thus, as the mental health community has not clearly determined that service dogs provide a benefit beyond dog ownership we conclude that equipoise exists; albeit individual providers may hold varying beliefs based on their own experiences. Certainly, the service dog community would have a bias as to the benefits of service dogs as compared to a pet dog. Patients with PTSD, however, may have different beliefs as several trials, including our Phase 1 and this trial (Phase 2), demonstrated differential dropout rates of usual care or EMOT relative to SERV. We did not quantify the degree of participant belief thus, this 'expectancy' of treatment outcomes may have contributed to group differences.

Additionally, strict blinding conditions were impractical, as once the dog type intervention was revealed the two treatment arms had different experiences during the pairing process. For example, the EMOT was delivered to the participant by the trainer with a brief period of introduction and care review conducted by the study team, whereas participants with a SERV travelled and spent up to two weeks, in some cases, on-site receiving detailed instructions. Masking the raters might have partially addressed the lack of true blinding, but this would have been difficult to implement given participants enjoyed talking about their dog and therefore, was

not done. In addition, we cannot simply reduce the intervention to differences in dog training, but rather any difference between the groups could reflect the additional programmatic differences in the pairing process. It is possible, despite the similarities of the post pairing experience (e.g., both arms had access to the same study team dog trainers, support for dog-related behaviors, veterinary access, etc.) that the initial differences in the pairing process impacted the outcome. We acknowledge the design limitations, lack of true blinding, differences in the intervention beyond just the enhanced training, and participant 'expectancy' as mechanistically influencing the reported differences between the groups to an unknown degree.

Another limitation (discussed at length in 1. Introduction E.ii) was that all subjects were paired with a dog thus no 'true control' group or placebo was achieved. Nonetheless, it is important to keep in mind that a placebo-controlled design not only would have created ethical challenges but could potentially have raised problems with an appropriate analysis as it introduces other biases that cannot be readily mitigated. During the design phase, comprehensive discussions were conducted with field experts and the study section, and ultimately it was determined that attrition from subjects assigned to either a 'waitlist' or 'usual care' would cripple enrollment targets as observed in prior studies. The initial study design sought to compare three interventions arms - SERV, EMOT, and usual care (no dog). Such a comparison would have allowed for a true comparison between the effect of the dog independent from the effect of the additional SERV training. The lack of a true control group limits our ability to disentangle the impact of dog ownership (whether SERV or EMOT) from the impact of PTSD treatment or time in general, but this concern is partially mitigated by the observation period (post-screening, pre-randomization to SERV vs EMOT). During the observation period, both study groups were without the presence of a dog and were assessed for primary and secondary outcome measures. However, within group change, pre-versus post-pairing, is not statistically valid as a measure of the effectiveness of the intervention. This is notable as prior studies have highlighted the physiological benefits of therapeutic animal presence (Viau, et al., 2010, Cooley & Barker, 2018). Our design did avoid that potential complication by using the EMOT as comparator group.

An additional potential limitation is that PTSD diagnosis as determined by CAPS-5 interview was not re-assessed prior to receiving the SERV intervention vs. EMOT intervention, and there may have been some participants who clinically improved during the time between enrollment and receiving the intervention such that they may not have met criteria for a PTSD diagnosis. The decision not to reassess for eligibility by PTSD diagnosis at that time was one that was deliberately made. Unlike other clinical trials (i.e. psychotherapeutic or pharmacologic), participants were very attached to the idea of receiving a dog, and we considered that it could have a detrimental impact on their mental health and therefore be potentially unethical to deny them a dog at this point in the study. Further, given the desire of the participants to receive their dog and a knowledge that meeting PTSD diagnostic criteria by CAPS interview was a requirement, we were concerned that this could falsely elevate PTSD symptom reporting at that time and introduce an additional confound into the study. Finally, we considered that this situation is analogous to that which would occur naturally in a setting in which SERV or EMOT dogs are provided to veterans. Given the complications associated with breeding and training dogs up to 2 years to specified tasks (or even to less rigorous obedience criteria for EMOTs), as in this study there will likely be a significant delay between initial acceptance to receive a dog and the time at which the dog is actually received. We remain firm in our conviction that it would be unacceptable to deny a participant receipt of a dog for which they initially qualified.

During the observation period, SI worsened as did the WHO-DAS 2.0, the VR-12 physical summary score, the PCL-5, and the DAR; while the VR-12 mental health summary score, PSQI, and PHQ-9 showed no discernable changes. Collectively, these data and the study team members' observations indicate a significant increase in observed anxiety and/or frustrations related to increasing time between baseline at study enrollment and the clearing. Certainly, ambiguity in the timing of the receipt of a dog and associations with self-reported scoring of WHO-DAS 2.0 and VR-12 may reflect individual levels of tolerances or frustrations related to prolonged wait periods of up to 9-12 months for some participants. These wait times reflect the significant challenges of trying to manage variations in participant recruiting rates with challenges in guaranteeing that vendors could produce trained, healthy dogs on a strict schedule. These challenges serve as a precaution to future study design when contemplating how best to structure the randomization and observation phases of a study.

It should also be noted that while we are assuming the most salient factors distinguishing the SERV intervention from the EMOT intervention are the trained tasks and public access, it is conceivable that some participants in the EMOT group took their dogs into public settings, despite the study parameters. Service dog fraud, when pet or emotional support dogs are taken into public places where they are not normally allowed, is an increasingly prevalent issue (Elliott & Hogle, 2013; Harpur, et al., 2018), and this would be consistent with behavior observed in the general public. If participants in the EMOT group did indeed do so, it is likely they would not have self-reported this behavior, and therefore it is not possible to determine whether or not this took place. Because the frequency of participants taking EMOT into public is not known, the impact of having a dog accompany the Veteran into public cannot be accurately ascertained from this study alone, and it is possible that the true variance between EMOT intervention and SERV intervention would be more dramatic if this were accounted for. Additionally, extra time and attention was given to those participants in the SERV intervention during the pairing phase of the study, which should not be discounted as a possible source of bias-particularly with respect to PTSD symptom improvement in the SERV intervention group.

We found about a two-fold higher rate of attrition in the EMOT arm of the study. Participants that withdrew when the dog type was revealed (at the clearing visit) were with one exception randomized to the EMOT group. This finding was unsurprising given the participant equipoise discussed previously and underlines the original decision to eliminate a "no-dog" control arm. In the majority of cases, participants assigned to the EMOT intervention group informally revealed their wish to receive a SERV, which would allow public access with their dog and the perceived benefit of the SERV trained tasks. However, no Veteran officially gave that reason for withdrawing after assignment to the EMOT group (see Table J). After learning of the EMOT assignment, these participants elected to drop out prior to pairing. On the other hand, some Veterans informally expressed relief that they received an EMOT dog because they did not want the public attention that accompanies having a SERV in public. Reasons for dropping out after pairing included inability to care for the dog, family deciding to withdraw from the study, and other reasons, which were uniquely attributed to individual Veterans. Nonetheless, consideration should be given to the profound influence that the glowing accounts of SERV successes popularized in media and by some service dog organizations have on Veterans who have not benefited from other therapies. In reality, pairing failures and dissatisfaction with mental health SERVs or other SERV types occur in all organizations but data on pairing failures are rarely released. What is

clear is that no service dog organization of any longevity can realistically claim a 100% paring success rate.

The VA dog course and the support provided to participants by the VA study site dog trainers were attempts to manage these inflated perceptions by emphasizing that each human/dog pair is unique and has emotional/recreational benefits. In trying to understand further why EMOT dog pairings were withdrawn more frequently, it is useful to consider the withdrawals in the EMOT and SERV groups before and after pairing. Withdrawals before pairings could not be based upon any actual differences in help provided by EMOT dogs versus SERV dogs because participants did not have their dogs at that time, while withdrawals after pairing could be due to differences in experiences with the dog type received.

Extrapolating how EMOT attrition rates would impact the findings is difficult. However, a key benefit of the SERV, as perceived by the participants, is public access as afforded by the protection of the ADA. The designers of the study were aware of this nuance and reminded participants of the ADA provisions at various points during the study. Our observations of participants' preferences also suggest that subjects anticipated more social engagement as a byproduct of receiving a service dog, a possible source of bias. As such, it could be interpreted that participants perceived that a protected ADA animal could better serve to address social isolation and the avoidance symptoms of PTSD. Further, the attrition rate found in the EMOT arm was greater than planned, potentially resulting in some comparisons being underpowered and inconclusive inferences.

Two other concerns, commonly associated with randomized controlled trials (RCT), are that the findings of the study may not be fully generalizable to the broader population of Veterans diagnosed with PTSD and that the lack of group differences over time with repeated measures could reflect regression to the mean.

Regarding generalizability, it is important to weigh the need to use a structured protocol and strict inclusion/exclusion criteria to maximize internal validity of the study results with potentially compromising external validity to the real-world practice setting (Kennedy-Martin, et al., 2015; Suskida, et al., 2018). In this study, Veterans enrolled were actively participating in mental health treatment within the VA setting and did not demonstrate comorbid psychosis, moderate or severe substance use disorders, active suicidal or homicidal ideation at the time of enrollment, recent psychiatric hospitalization, or active documentation of disruptive behavior, suggesting that the study population exhibited overall less severe psychiatric impairment and comorbidity. However, these severe symptoms would likely also disqualify a Veteran from receiving a SERV from a typical service dog organization due to concerns about ability to care for the dog.

Beyond these clinical parameters, enrolled Veterans could not own other dogs or pets that might impede bonding with the SERV or EMOT, but had to be capable of looking after a dog, had to have a stable home suitable for a dog, and could not have children in the home under 5 years of age, thereby narrowing the subset of Veterans who could be enrolled. As such, the findings of this study, both in terms of clinical outcomes and adverse effects, may not extrapolate directly to the larger populations of Veterans with PTSD when utilized as a clinical intervention in standard practice.

Of note, we did not characterize data on VA clinical care for PTSD. It is possible that care was differentially distributed and could have influenced outcomes. It is also possible that appointment attendance and therapeutic adherence could have been influenced by study assignment. If this were the case, we would expect this to be in favor of the SERV group. Since PTSD symptom reduction is the focus of PTSD treatment, if there were differential attendance and adherence in favor of the Veterans with SERVs, it is possible that this may been causal in the PTSD symptom reduction finding.

Observations of the data did suggest an initial substantial improvement in functioning and disability measures upon receipt of the intervention. In trials, such findings when repeated have a tendency to regress to the mean, Thus it is possible that given the duration of the trial and multiple measurement points combined with the natural course of PTSD (clinically it is marked by relapses and remissions), the lack of observed group differences may reflect this phenomena.

Finally, due to the nature of the study design, all participants were required to stay in active treatment engagement with their assigned MH team (requirements were the same between the two interventions). Active treatment engagement defined as their mental health care treatment as usual, and this concurrent PTSD treatment, including medications and/or therapy, was not controlled for over the course of the study. This usual care study design requirement may have also contributed to improvements in PTSD functioning and disability secondary to adherence with MH care. As noted previously, it would be unethical to ask participants to stop utilizing their existing PTSD therapies to allow a comparison of an unproven potential mitigation for PTSD; therefore, the impact of ongoing usual care treatment on the interpretation of the study cannot be readily quantified.

C. Conclusions

This study is the most comprehensive and scientifically rigorous examination of the impact of two different types of dog interventions on PTSD related to disability and functioning. Though there were no significant differences between the SERV and EMOT interventions on the primary outcomes or multiple other secondary outcomes, this research did demonstrate within-group improvements for both interventions and between group benefits for the SERV intervention for PTSD symptom burden. This reduction in PTSD symptoms for participants who received the SERV intervention placed mean scores very close to the cutoff point for less need for clinical intervention, suggesting a SERV intervention advantage over an EMOT intervention. The advantages of a participant receiving a SERV as compared to a participant with an EMOT from a PTSD clinical perspective are likely to be more nuanced as they relate to individuals, as is often the case when applying differences in means to individual recommendations. The results of this study add to a growing body of literature indicating that a SERV, as an adjunct to usual care, does not appear to worsen functioning or to demonstrably impede extinction of fear conditioning by acting as a safety behavior.

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8. APPENDICES

The following Appendices are provided:

Appendix A: Listing and Description of Study Forms

Appendix B: Additional Mental Health Results

Part A – Additional Models

Part B – Attrition and Missing Data Analyses

Appendix A- Listing and Description of Study Forms

Table YY. Listing and description of study forms. All forms are available on the web: https://www.research.va.gov/programs/animal_research/PTSDstudy.cfm.

Form Number	Title	Use
01	Demographics	Completed for each participant during screening to capture demographic data; 4 pages
03	CAPS 5 Summary Sheet	Records CAPS instrument responses to document diagnosis of PTSD; 3 pages
04	MINI Screen (Version 7.0.0 for DSM-5)	Records responses to MINI screen instrument; 2 pages
05	Suitability to Have a Dog Checklist	Captures relevant safety information on participant's home to help ensure dog safety once paired; 5 pages
07	WHO-DAS 2.0	Records responses to WHO-DAS 2.0 instrument; 4 pages
08	PCL-5	Records responses to PCL-5 instrument; 2 pages
09	Pittsburgh Sleep Quality Index (PSQI)	Records responses to PSQI instrument; 3 pages
10	VR-12	Records responses to VR-12 instrument; 3 pages
11	Columbia- Suicide Severity Rating Scale	Records responses to C-SSRS instrument; 6 pages
12	PHQ-9	Records responses to PHQ-9 instrument; 1 page
13	Dimension of Anger Reactions Assessment	Records responses to Dimensions of Anger Reactions instrument; 1 page
14	Non-VA Inpatient and Outpatient Care	Used by the VA Health Economics Research Center to capture healthcare utilization data; 3 pages
15	Work Productivity and Activity Impairment Questionnaire: General Health V2.0	Used by VA Health Economics Research Center to capture responses to WPAI:GH v2.0 instrument; 2 pages
16	Inclusion/Exclusion	Used to screen participants for inclusion and exclusion criteria; 3 pages
17	Prior/Concomitant Medications Log	Used by VA Health Economics Research Center to capture medication usage data; 2 pages
18	Payment Log	Used to track study reimbursements to participants; 2 pages
19	Post-Pairing Evaluation	Used to monitor the health of the pairing and record any participant concerns for follow-up by a VA dog trainer; 5 pages
20	Veteran and Service/Emotional Support Dog Visit Report	Used to document non-routine support visits by VA dog trainers to assist participants; 3 pages
21	Dog Related Questions	Used to document additional details of routine and non-routine visits by VA dog trainers; 6 pages

22	Intervention Discontinuation (Dog Return) Form	Used to document temporary or permanent return of paired dogs to VA; 2 pages
23	Veterinarian Checklist	Used to document required periodic visits to veterinary clinics by participants with their dogs; 5 pages
24	Study Completion/Termination	Captures reason for participant withdrawing from study; 2 pages
24a	Final Interview - Service Dogs	Captures information during final interview of participant paired with a service dog before completing the study; 6 pages
24b	Final Interview - Emotional Support Dogs	Captures information during final interview of participant paired with an emotional support dog before completing the study; 7 pages
24c	Dog Trainer Evaluation	Used by VA dog trainers to independently evaluate retention of obedience commands and service dog tasks as participants exit the study; 1 page
25	Protocol Deviation	Records any protocol deviations for remediation or mitigation; 3 pages
26	Adverse Event (AE)	Documents participant adverse events; 2 pages
26a	Adverse Event (AE) for Dog	Documents dog adverse events; 2 pages
27	Serious Adverse Event (SAE)	Documents participant serious adverse events; 3 pages
27a	Serious Adverse Event (SAE) for Dogs	Documents dog serious adverse events; 3 pages
28	Serious Adverse Event (SAE) Follow-Up	Documents actions taken after a participant serious adverse event; 2 pages
28a	Serious Adverse Event (SAE) Follow-Up for Dog	Documents actions taken after a dog serious adverse event; 2 pages
86	Informed Consent Confirmation	Records information related to the participant signing the study informed consent document, and being referred by a VA mental health provider; 1 page

Appendix B: Additional Mental Health Results

Part A – Additional Models

Table ZZ. Demographics for Participants Paired with a Study Dog by Medical Center

		Atlanta (n= 69)	Iowa City (n= 69)	Portland (n= 43)	Total (n=181)
Age (years)	n	69	69	43	181
	Mean (SD)	51.6 (11.84)	51.8 (14.63)	47.0 (14.24)	50.6 (13.61)
	Median	52.0	53.0	48.0	51.0
	Min, Max	28, 76	22, 79	24, 74	22, 79
Gender	n	69	69	43	181
Male	n (%)	54 (78.3)	59 (85.5)	32 (74.4)	145 (80.1)
Female	n (%)	15 (21.7)	10 (14.5)	11 (25.6)	36 (19.9)
Race	n	69	69	43	181
American Indian or Alaskan Native	n (%)	0 (0.0)	2 (2.9)	1 (2.3)	3 (1.7)
Asian	n (%)	1 (1.4)	0 (0.0)	1 (2.3)	2 (1.1)
Black, or African-American	n (%)	17 (24.6)	3 (4.3)	2 (4.7)	22 (12.2)
Native Hawaiian or Pacific Islander	n (%)	0 (0.0)	0 (0.0)	1 (2.3)	1 (0.6)
White	n (%)	26 (37.7)	59 (85.5)	35 (81.4)	120 (66.3)
Unknown	n (%)	0 (0.0)	0 (0.0)	1 (2.3)	1 (0.6)
Other	n (%)	0 (0.0)	0 (0.0)	1 (2.3)	1 (0.6)
Multiple Races	n (%)	25 (36.2)	5 (7.2)	1 (2.3)	31 (17.1)
Ethnicity	n	69	69	43	181
Hispanic	n (%)	6 (8.7)	2 (2.9)	4 (9.3)	12 (6.6)
Not Hispanic	n (%)	63 (91.3)	64 (92.8)	38 (88.4)	165 (91.2)
Unknown	n (%)	0 (0.0)	3 (4.3)	1 (2.3)	4 (2.2)
Marital Status	n	69	69	43	181
Married	n (%)	26 (37.7)	28 (40.6)	15 (34.9)	69 (38.1)
Co-habitating	n (%)	3 (4.3)	6 (8.7)	0 (0.0)	9 (5.0)
Widowed	n (%)	2 (2.9)	3 (4.3)	0 (0.0)	5 (2.8)
Never Married	n (%)	5 (7.2)	6 (8.7)	13 (30.2)	24 (13.3)
Divorced	n (%)	29 (42.0)	22 (31.9)	14 (32.6)	65 (35.9)
Separated	n (%)	4 (5.8)	4 (5.8)	1 (2.3)	9 (5.0)
Education Level	n	69	69	43	181
< High School Diploma	n (%)	1 (1.4)	2 (2.9)	0 (0.0)	3 (1.7)
High School Diploma/GED	n (%)	13 (18.8)	16 (23.2)	1 (2.3)	30 (16.6)
Some College Credit	n (%)	27 (39.1)	30 (43.5)	15 (34.9)	72 (39.8)
Associate Degree	n (%)	11 (15.9)	10 (14.5)	10 (23.3)	31 (17.1)
Bachelor's Degree	n (%)	8 (11.6)	5 (7.2)	10 (23.3)	23 (12.7)
Master's Degree	n (%)	9 (13.0)	3 (4.3)	7 (16.3)	19 (10.5)
Ph.D. or Professional Degree	n (%)	0 (0.0)	3 (4.3)	0 (0.0)	3 (1.7)
Income Level	n	69	69	43	181
< $10,000	n (%)	3 (4.3)	4 (5.8)	3 (7.0)	10 (5.5)
$10,001 - $20,000	n (%)	6 (8.7)	9 (13.0)	10 (23.3)	25 (13.8)
$20,001 - $30,000	n (%)	6 (8.7)	8 (11.6)	11 (25.6)	25 (13.8)
$30,001 - $40,000	n (%)	12 (17.4)	14 (20.3)	3 (7.0)	29 (16.0)
$40,001 - $50,000	n (%)	11 (15.9)	13 (18.8)	5 (11.6)	29 (16.0)
$50,001 - $60,000	n (%)	13 (18.8)	8 (11.6)	7 (16.3)	28 (15.5)
$60,001 - $70,000	n (%)	11 (15.9)	6 (8.7)	2 (4.7)	19 (10.5)
> $70,001	n (%)	7 (10.1)	6 (8.7)	2 (4.7)	15 (8.3)
Missing	n (%)	0 (0.0)	1 (1.4)	0 (0.0)	1 (0.6)
Walk Outside	n	69	69	43	181
Never	n (%)	0 (0.0)	10 (14.5)	4 (9.3)	14 (7.7)
One or time times a week	n (%)	14 (20.3)	15 (21.7)	11 (25.6)	40 (22.1)
At least once a day	n (%)	33 (47.8)	27 (39.1)	26 (60.5)	86 (47.5)
More than once a day	n (%)	22 (31.9)	15 (21.7)	2 (4.7)	39 (21.5)

		Atlanta (n= 69)	Iowa City (n= 69)	Portland (n= 43)	Total (n=181)
Missing	n (%)	0 (0.0)	2 (2.9)	0 (0.0)	2 (1.1)
Served Outside US	n	69	69	43	181
No	n (%)	2 (2.9)	5 (7.2)	7 (16.3)	14 (7.7)
Yes	n (%)	67 (97.1)	64 (92.8)	36 (83.7)	167 (92.3)
Served in Combat Area	n	69	69	43	181
No	n (%)	17 (24.6)	16 (23.2)	14 (32.6)	47 (26.0)
Yes	n (%)	52 (75.4)	53 (76.8)	29 (67.4)	134 (74.0)
Hearing Impairment	n	69	69	43	181
No	n (%)	34 (49.3)	37 (53.6)	24 (55.8)	95 (52.5)
Yes	n (%)	35 (50.7)	31 (44.9)	19 (44.2)	85 (47.0)
Missing	n (%)	0 (0.0)	1 (1.4)	0 (0.0)	1 (0.6)
Visual Impairment	n	69	69	43	181
No	n (%)	61 (88.4)	60 (87.0)	28 (65.1)	149 (82.3)
Yes	n (%)	8 (11.6)	9 (13.0)	15 (34.9)	32 (17.7)
Mobility Impairment	n	69	69	43	181
No	n (%)	37 (53.6)	48 (69.6)	31 (72.1)	116 (64.1)
Yes	n (%)	32 (46.4)	20 (29.0)	12 (27.9)	64 (35.4)
Missing	n (%)	0 (0.0)	1 (1.4)	0 (0.0)	1 (0.6)
Alternative Therapy	n	69	69	43	181
No	n (%)	43 (62.3)	53 (76.8)	17 (39.5)	113 (62.4)
Yes	n (%)	26 (37.7)	16 (23.2)	26 (60.5)	68 (37.6)
Branch of Military	n	69	69	43	181
Army	n (%)	41 (59.4)	30 (43.5)	25 (58.1)	96 (53.0)
Navy	n (%)	9 (13.0)	11 (15.9)	9 (20.9)	29 (16.0)
Air Force	n (%)	6 (8.7)	6 (8.7)	5 (11.6)	17 (9.4)
Marines	n (%)	16 (23.2)	20 (29.0)	5 (11.6)	41 (22.7)
Coast Guard	n (%)	0 (0.0)	0 (0.0)	2 (4.7)	2 (1.1)
Merchant Marines	n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
National Guard	n (%)	10 (14.5)	5 (7.2)	5 (11.6)	20 (11.0)
When Served	n	69	69	43	181
World War I	n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
World War II	n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Korean conflict	n (%)	0 (0.0)	1 (1.4)	0 (0.0)	1 (0.6)
Vietnam conflict	n (%)	13 (18.8)	25 (36.2)	12 (27.9)	50 (27.6)
Gulf War	n (%)	27 (39.1)	17 (24.6)	9 (20.9)	53 (29.3)
Balkans conflict	n (%)	3 (4.3)	1 (1.4)	0 (0.0)	4 (2.2)
Afghanistan conflict	n (%)	11 (15.9)	9 (13.0)	10 (23.3)	30 (16.6)
Iraq conflict	n (%)	16 (23.2)	26 (37.7)	19 (44.2)	61 (33.7)
Peace time	n (%)	26 (37.7)	8 (11.6)	4 (9.3)	38 (21.0)
Other conflict	n (%)	16 (23.2)	5 (7.2)	0 (0.0)	21 (11.6)
Work Status	n	69	69	43	181
Working part or full time	n (%)	9 (13.0)	27 (39.1)	15 (34.9)	51 (28.2)
Student full time	n (%)	1 (1.4)	4 (5.8)	11 (25.6)	16 (8.8)
Student part time	n (%)	1 (1.4)	1 (1.4)	3 (7.0)	5 (2.8)
Homemaker	n (%)	0 (0.0)	2 (2.9)	0 (0.0)	2 (1.1)
Retired not due to disability	n (%)	14 (20.3)	12 (17.4)	6 (14.0)	32 (17.7)
Volunteer full time	n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Volunteer part time	n (%)	5 (7.2)	6 (8.7)	4 (9.3)	15 (8.3)
Disabled: unable to work due to physical disability	n (%)	42 (60.9)	11 (15.9)	7 (16.3)	60 (33.1)
Disabled: unable to work due to mental health status	n (%)	47 (68.1)	21 (30.4)	10 (23.3)	78 (43.1)
Unemployed and not seeking work	n (%)	1 (1.4)	7 (10.1)	5 (11.6)	13 (7.2)
Unemployed actively seeking work	n (%)	0 (0.0)	1 (1.4)	3 (7.0)	4 (2.2)
Other work status	n (%)	0 (0.0)	3 (4.3)	0 (0.0)	3 (1.7)

Table AAA. Unadjusted WHO-DAS 2.0 Domain Scores (lower score = less disability) over time by group (PP)

Cognition

	EMOT						SERV					
Visits	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**
Baseline	84	36.25	18.08	0	95	35	97	35.98	20.20	0	100	35
Cleared	84	43.87	18.94	0	90	45	97	41.39	19.43	0	90	45
Month 3	76	40.33	17.04	0	70	40	95	38.16	17.31	0	80	40
Month 6	73	38.84	17.98	0	90	40	94	36.01	16.65	5	70	35
Month 9	70	41.29	19.59	0	100	40	92	36.50	18.23	0	80	35
Month 12	68	38.47	17.81	0	85	40	90	35.10	18.68	0	80	30
Month 15	66	40.15	19.21	0	90	40	89	33.43	19.26	0	80	30
Month 18	65	34.85	18.35	0	70	35	88	32.22	17.08	0	80	30

Mobility

	EMOT						SERV					
Visits	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**
Baseline	84	30.98	23.27	0	87.5	28.15	97	25.60	22.81	0	93.8	18.8
Cleared	84	39.90	22.00	0	93.8	43.8	97	34.63	23.18	0	93.8	37.5
Month 3	76	37.36	22.78	0	87.5	37.5	95	33.23	23.02	0	81.3	31.3
Month 6	73	40.52	25.18	0	100	43.8	94	35.06	25.18	0	93.8	37.5
Month 9	70	41.28	24.76	0	100	43.8	92	34.33	24.23	0	100	37.5
Month 12	68	38.72	24.03	0	87.5	43.8	90	34.14	24.29	0	100	31.3
Month 15	66	43.58	26.25	0	100	43.8	89	33.37	25.07	0	87.5	31.3
Month 18	65	37.14	22.73	0	81.3	37.5	88	31.91	24.44	0	87.5	31.3

Self-Care

	EMOT						SERV					
Visits	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**
Baseline	84	14.76	18.98	0	80	10	97	13.51	18.03	0	60	10
Cleared	84	19.76	20.59	0	90	10	97	20.00	20.67	0	80	10
Month 3	76	20.39	20.36	0	80	10	95	17.68	19.32	0	70	10
Month 6	73	20.68	21.37	0	80	20	94	16.49	18.65	0	80	10
Month 9	70	24.00	22.22	0	100	20	92	17.61	20.62	0	70	10
Month 12	68	20.34	20.59	0	80	20	90	19.22	20.57	0	80	10
Month 15	66	22.63	20.92	0	70	20	89	17.42	19.10	0	70	10
Month 18	65	19.23	19.79	0	70	10	88	16.70	18.55	0	60	10

Interpersonal Interactions

	EMOT						SERV					
Visits	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**
Baseline	83	50.86	23.40	0	100	50	97	51.81	22.58	0	100	50
Cleared	84	56.45	23.97	0	100	58.3	97	56.76	23.63	0	100	58.3
Month 3	76	51.53	22.60	0	100	50	95	53.16	21.31	0	100	50
Month 6	73	51.71	21.83	0	100	50	94	46.37	22.52	0	100	45.85
Month 9	70	50.42	23.34	0	100	50	92	48.46	19.81	0	100	50
Month 12	68	47.52	23.03	0	100	50	90	46.16	21.44	0	91.7	41.7
Month 15	66	53.82	23.90	0	100	50	89	48.71	20.26	0	100	50
Month 18	65	48.40	26.37	0	100	50	88	41.65	22.67	0	100	41.7

Life Activities – Domestic

	EMOT						SERV					
Visits	**n**	**SERV**	**SD**	**Min**	**Max**	**Median**	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**
Baseline	84	39.88	24.71	0	100	40	97	35.26	25.00	0	100	40
Cleared	84	46.90	27.33	0	100	50	97	44.74	25.25	0	100	50
Month 3	76	48.82	25.08	0	100	50	95	41.05	26.84	0	100	40
Month 6	73	47.12	25.14	0	100	50	94	41.38	25.34	0	100	40
Month 9	70	48.95	26.02	0	100	50	92	42.28	23.54	0	100	40
Month 12	68	48.97	25.87	0	100	50	90	42.52	23.27	0	100	45
Month 15	66	50.45	26.74	0	100	50	88	40.45	27.12	0	100	40
Month 18	65	45.38	25.44	0	100	40	88	37.84	24.89	0	100	40

Life Activities – Work, School

	EMOT						SERV					
Visits	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**
Baseline	42	37.08	18.55	0	78.6	35.7	53	34.51	29.21	0	100	28.6
Cleared	46	48.29	25.25	0	100	50	47	39.57	20.84	0	92.9	42.9
Month 3	40	47.15	22.81	0	100	42.9	45	35.88	23.32	0	92.9	35.7
Month 6	32	43.53	24.77	0	100	42.9	40	28.40	21.50	0	78.6	28.6
Month 9	31	48.24	25.93	0	100	50	38	28.20	21.97	0	85.7	28.6
Month 12	28	39.54	23.12	0	100	35.7	45	34.82	23.43	0	85.7	28.6
Month 15	33	46.47	23.55	0	100	42.9	42	34.01	21.74	0	71.4	35.7
Month 18	30	35.23	22.50	0	85.7	32.15	46	32.92	21.00	0	78.6	32.15

Participation in Society

	EMOT						SERV					
Visits	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**
Baseline	84	56.49	19.55	0	100	56.25	97	51.98	19.71	8.3	91.7	50
Cleared	84	55.46	20.94	4.2	95.8	54.2	97	54.51	19.85	4.2	95.8	58.3
Month 3	76	49.76	19.50	0	87.5	50	95	48.37	19.41	0	100	45.8
Month 6	73	50.00	19.40	0	100	54.2	94	45.76	18.50	0	95.8	45.8
Month 9	70	49.65	19.46	4.2	100	50	92	43.21	19.58	0	100	45.8
Month 12	68	49.57	19.50	4.2	100	50	90	43.15	18.58	0	83.3	41.7
Month 15	66	48.26	20.18	0	95.8	45.8	89	42.47	19.83	0	100	41.7
Month 18	65	43.85	21.59	0	87.5	41.7	88	39.44	20.11	4.2	100	37.5

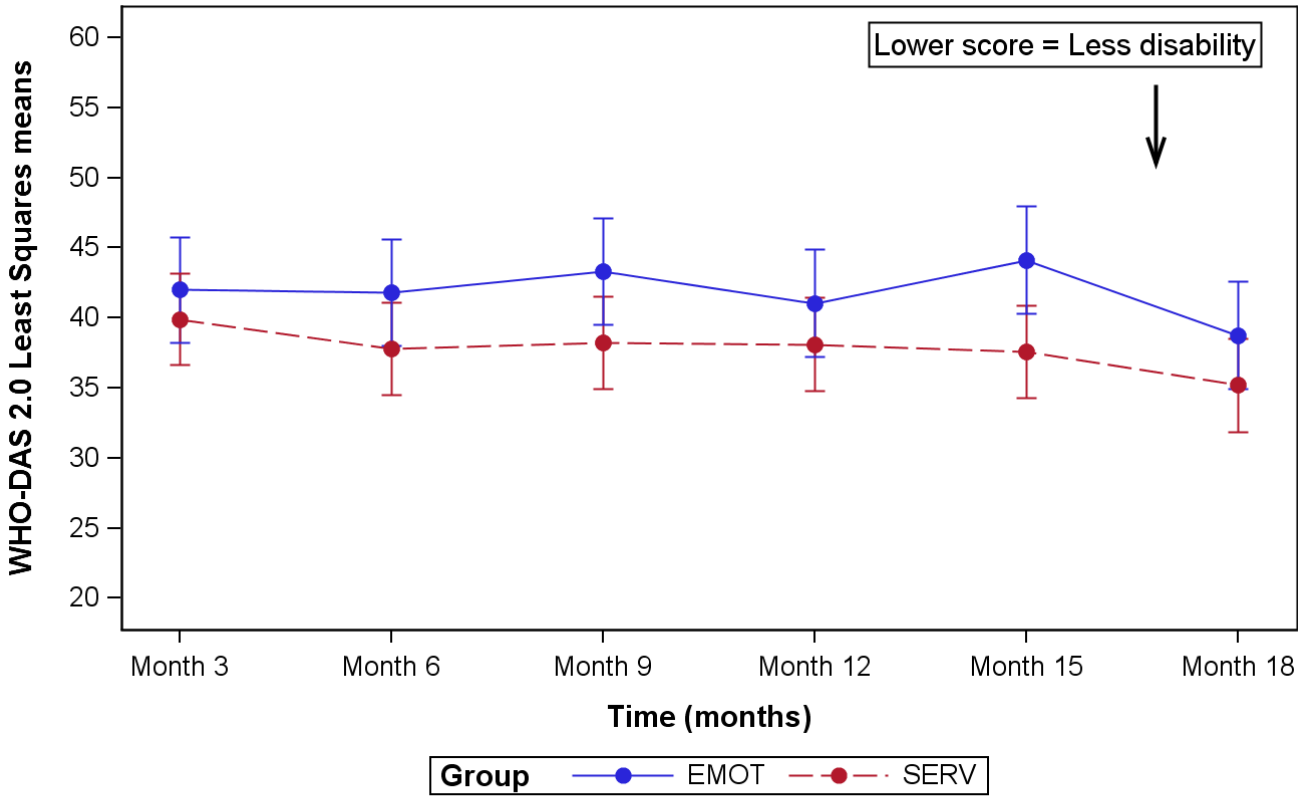
Table BBB. Random Intercept model results for WHO-DAS 2.0 (PP)

		Random Int (PP)	
Outcome	**Effect**	**F statistic**	**P-value**
WHO-DAS 2.0	Baseline score	62.02	<.0001
	Gender	2.11	0.1483
	Center	7.81	0.0006
	Treatment	4.04	0.0462
	Time	5.36	<.0001
	Treatment*Time	1.51	0.1846

Table CCC. Effect of SERV Intervention vs. EMOT Intervention for WHO-DAS 2.0 (PP)

	Outcome Measure	Population-Model Type	PP			
			Estimate	95% CI Lower	95% CI Upper	P-value
SERV vs. EMOT over time	WHO-DAS 2.0	random intercept	-4.0386	-8.0075	-0.06959	0.0462
SERV vs. EMOT at 18 months	WHO-DAS 2.0	random intercept	-3.5742	-8.2034	1.0551	0.1297

Figure CCC.2. WHO-DAS 2.0 overall summary score Least Squares Means and 95% confidence intervals over time by Treatment from the random intercept model (lower score=improvement; PP population)



Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

Table CCC.3. WHO-DAS 2.0 overall summary score Least Squares Means (Adjusted) and 95% confidence intervals over time by Treatment from the random intercept model (lower score=improvement; PP population)

	EMOT		SERV	
Time	**N**	**Adjusted Mean (95% CI)**	**N**	**Adjusted Mean (95% CI)**
3	76	42.00 (38.25, 45.75)	95	39.90 (36.63, 43.17)
6	73	41.80 (38.02, 45.57)	94	37.80 (34.52, 41.08)
9	70	43.33 (39.53, 47.13)	92	38.24 (34.95, 41.54)
12	68	41.05 (37.23, 44.87)	90	38.11 (34.81, 41.42)
15	66	44.11 (40.27, 47.94)	88	37.57 (34.26, 40.89)
18	65	38.76 (34.91, 42.61)	88	35.18 (31.87, 38.50)

Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

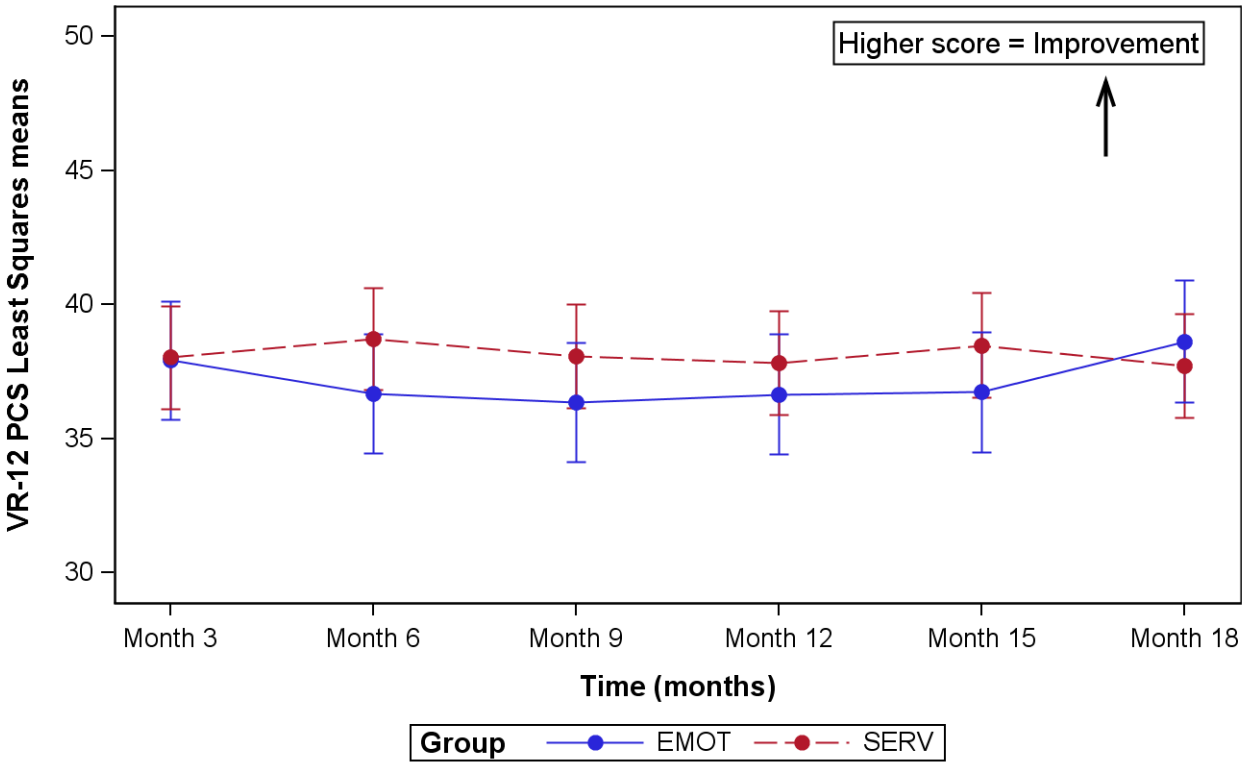
Table DDD. Random Intercept model results for the VR-12 (PP)

		Random Int (PP)	
Outcome	**Effect**	**F statistic**	**P-value**
VR-12 PCS	Baseline score	161.46	<.0001
	Gender	0.38	0.5372
	Center	0.70	0.4989
	Treatment	0.73	0.3941
	Time	0.83	0.5297
	Treatment*Time	1.83	0.1054
VR-12 MCS	Baseline score	68.57	<.0001
	Gender	3.31	0.0708
	Center	4.59	0.0115
	Treatment	0.22	0.6362
	Time	6.70	<.0001
	Treatment*Time	1.33	0.2488

Table EEE.1. Effect of SERV Intervention vs. EMOT Intervention for VR-12 (PP)

	Outcome Measure	Population -Model Type	PP			
			Estimate	**95% CI Lower**	**95% CI Upper**	**P-value**
SERV vs. EMOT over time	VR-12 PCS	random intercept	0.9768	-1.2801	3.2338	0.3941
SERV vs. EMOT at 18 months	VR-12 PCS	random intercept	-0.9066	-3.6580	1.8448	0.5174
SERV vs. EMOT over time	VR-12 MCS	random intercept	0.5269	-1.6686	2.7223	0.6362
SERV vs. EMOT at 18 months	VR-12 MCS	random intercept	1.3241	-1.6241	4.2722	0.3779

Figure EEE.2. VR-12 PCS summary score Least Squares Means and 95% confidence intervals over time by Treatment from the random intercept model (higher score=improvement; population)



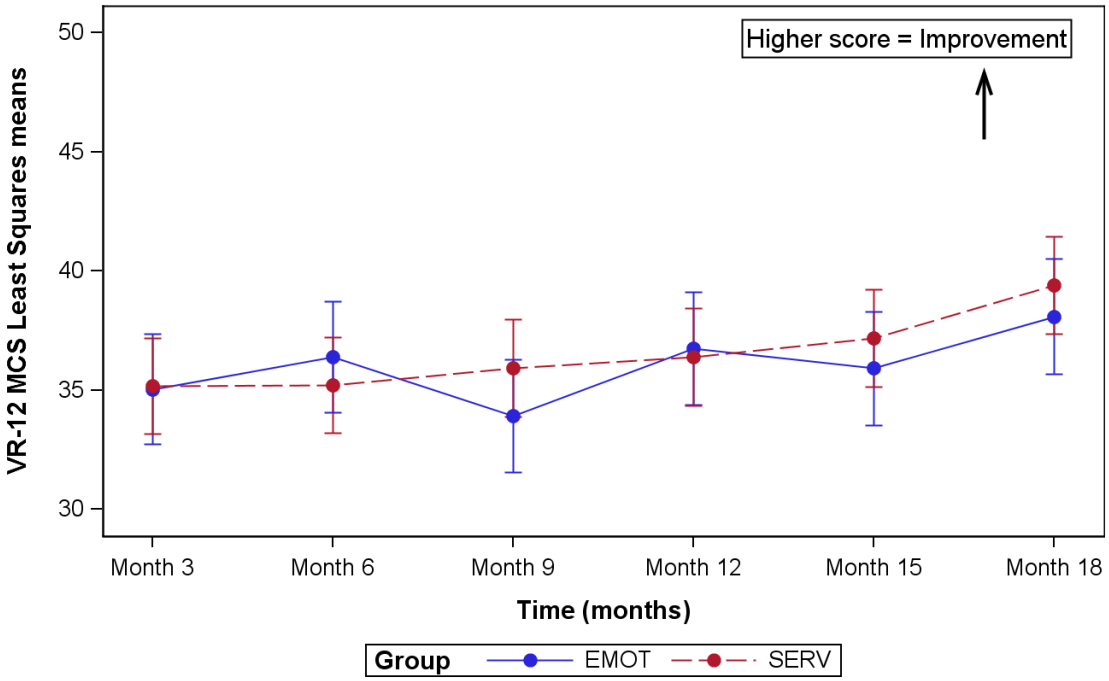
Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

Table EEE.3. VR-12 PCS summary score Least Squares Means (Adjusted) and 95% confidence intervals over time by Treatment from the random intercept model (higher score=improvement; PP population)

	EMOT		SERV	
Time	**N**	**Adjusted Mean (95% CI)**	**N**	**Adjusted Mean (95% CI)**
3	75	37.91 (35.72, 40.10)	94	38.02 (36.11, 39.93)
6	71	36.67 (34.46, 38.88)	94	38.72 (36.80, 40.63)
9	69	36.36 (34.13, 38.59)	89	38.07 (36.13, 40.00)
12	68	36.65 (34.41, 38.89)	89	37.81 (35.88, 39.74)
15	66	36.73 (34.48, 38.98)	87	38.48 (36.54, 40.42)
18	63	38.63 (36.36, 40.89)	87	37.72 (35.78, 39.66)

Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

Figure EEE.4. VR-12 MCS summary score Least Squares Means and 95% confidence intervals over time by Treatment from the random intercept model (higher score=improvement; PP population population)



Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

Table EEE.5. VR-12 MCS summary score Least Squares Means (Adjusted) and 95% confidence intervals over time by Treatment from the random intercept model (higher score=improvement; PP population)

	EMOT		SERV	
Time	**N**	**Adjusted Mean (95% CI)**	**N**	**Adjusted Mean (95% CI)**
3	75	35.04 (32.74, 37.34)	94	35.18 (33.18, 37.18)
6	71	36.40 (34.07, 38.73)	94	35.20 (33.19, 37.21)
9	69	33.92 (31.56, 36.27)	89	35.93 (33.89, 37.97)
12	68	36.76 (34.39, 39.13)	89	36.39 (34.35, 38.43)
15	66	35.92 (33.53, 38.30)	87	37.18 (35.13, 39.23)
18	63	38.08 (35.67, 40.49)	87	39.41 (37.36, 41.45)

Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

Table FFF. Unadjusted PSQI Components (lower score = better) over time by group (PP)

Sleep Quality

	EMOT						SERV					
Visits	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**
Baseline	84	2.21	0.76	0.00	3.00	2.00	97	2.04	0.71	1.00	3.00	2.00
Cleared	84	2.06	0.83	0.00	3.00	2.00	97	2.07	0.74	1.00	3.00	2.00
Month 3	76	1.91	0.98	0.00	3.00	2.00	95	1.74	0.81	0.00	3.00	2.00
Month 6	73	1.86	0.82	0.00	3.00	2.00	94	1.70	0.72	1.00	3.00	2.00
Month 9	70	1.77	0.90	0.00	3.00	2.00	92	1.73	0.80	0.00	3.00	2.00
Month 12	68	1.91	0.89	0.00	3.00	2.00	90	1.71	0.71	1.00	3.00	2.00
Month 15	66	1.79	0.92	0.00	3.00	2.00	89	1.74	0.72	1.00	3.00	2.00
Month 18	65	1.74	0.78	0.00	3.00	2.00	88	1.58	0.81	0.00	3.00	1.00

Sleep Latency

	EMOT						SERV					
Visits	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**
Baseline	84	2.24	0.96	0.00	3.00	3.00	96	2.26	0.91	0.00	3.00	3.00
Cleared	83	2.42	0.84	0.00	3.00	3.00	97	2.37	0.83	0.00	3.00	3.00
Month 3	76	2.30	0.86	0.00	3.00	3.00	95	2.01	1.07	0.00	3.00	2.00
Month 6	73	2.23	0.91	0.00	3.00	3.00	94	2.07	0.92	0.00	3.00	2.00
Month 9	70	2.17	0.90	0.00	3.00	2.00	92	2.00	1.01	0.00	3.00	2.00
Month 12	68	2.18	0.96	0.00	3.00	2.00	90	2.02	1.08	0.00	3.00	2.00
Month 15	65	2.15	0.97	0.00	3.00	2.00	89	2.03	1.03	0.00	3.00	2.00
Month 18	65	2.03	1.05	0.00	3.00	2.00	88	1.97	1.02	0.00	3.00	2.00

Sleep Duration

	EMOT						SERV					
Visits	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**
Baseline	84	2.00	1.06	0.00	3.00	2.00	97	1.80	1.11	0.00	3.00	2.00
Cleared	84	1.79	1.18	0.00	3.00	2.00	97	1.75	1.12	0.00	3.00	2.00
Month 3	76	1.68	1.19	0.00	3.00	2.00	95	1.54	1.16	0.00	3.00	2.00
Month 6	73	1.59	1.22	0.00	3.00	2.00	94	1.45	1.13	0.00	3.00	1.00
Month 9	70	1.69	1.14	0.00	3.00	2.00	92	1.63	1.14	0.00	3.00	2.00
Month 12	68	1.71	1.15	0.00	3.00	2.00	90	1.66	1.20	0.00	3.00	2.00
Month 15	66	1.68	1.13	0.00	3.00	2.00	89	1.54	1.12	0.00	3.00	2.00
Month 18	65	1.45	1.12	0.00	3.00	2.00	88	1.55	1.12	0.00	3.00	1.50

Habitual Sleep Efficiency

	EMOT						SERV					
Visits	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**
Baseline	84	1.85	1.25	0.00	3.00	2.00	96	1.81	1.27	0.00	3.00	2.00
Cleared	84	2.02	1.13	0.00	3.00	2.00	97	1.72	1.25	0.00	3.00	2.00
Month 3	76	1.95	1.15	0.00	3.00	2.00	95	1.77	1.21	0.00	3.00	2.00
Month 6	73	1.70	1.21	0.00	3.00	2.00	94	1.61	1.20	0.00	3.00	1.50
Month 9	70	1.71	1.28	0.00	3.00	2.00	92	1.65	1.21	0.00	3.00	2.00
Month 12	68	1.75	1.19	0.00	3.00	2.00	90	1.68	1.22	0.00	3.00	2.00
Month 15	66	1.80	1.26	0.00	3.00	2.00	89	1.69	1.27	0.00	3.00	1.00
Month 18	65	1.82	1.13	0.00	3.00	2.00	88	1.60	1.26	0.00	3.00	1.50

Sleep Disturbance

	EMOT						SERV					
Visits	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**
Baseline	84	2.37	0.67	1.00	3.00	2.00	96	2.30	0.65	1.00	3.00	2.00
Cleared	83	2.43	0.63	1.00	3.00	3.00	97	2.34	0.68	1.00	3.00	2.00
Month 3	75	2.40	0.74	0.00	3.00	3.00	95	2.15	0.70	1.00	3.00	2.00
Month 6	73	2.27	0.71	0.00	3.00	2.00	94	2.14	0.67	1.00	3.00	2.00
Month 9	69	2.29	0.67	1.00	3.00	2.00	91	2.14	0.66	0.00	3.00	2.00
Month 12	68	2.21	0.70	1.00	3.00	2.00	90	1.99	0.66	1.00	3.00	2.00
Month 15	65	2.20	0.67	1.00	3.00	2.00	88	2.02	0.71	1.00	3.00	2.00
Month 18	65	2.17	0.72	1.00	3.00	2.00	87	2.07	0.71	1.00	3.00	2.00

Use of Sleep Medication

	EMOT						SERV					
Visits	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**
Baseline	84	1.93	1.34	0.00	3.00	3.00	97	1.87	1.34	0.00	3.00	3.00
Cleared	84	2.04	1.31	0.00	3.00	3.00	97	1.92	1.36	0.00	3.00	3.00
Month 3	76	1.83	1.36	0.00	3.00	3.00	95	1.84	1.39	0.00	3.00	3.00
Month 6	73	1.86	1.39	0.00	3.00	3.00	94	1.74	1.41	0.00	3.00	3.00
Month 9	70	1.99	1.25	0.00	3.00	3.00	92	1.75	1.40	0.00	3.00	3.00
Month 12	68	1.90	1.41	0.00	3.00	3.00	90	1.71	1.40	0.00	3.00	2.50
Month 15	66	1.95	1.33	0.00	3.00	3.00	89	1.62	1.37	0.00	3.00	2.00
Month 18	65	1.94	1.33	0.00	3.00	3.00	88	1.65	1.35	0.00	3.00	2.00

Daytime Dysfunction

	EMOT						SERV					
Visits	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**
Baseline	84	1.67	0.80	0.00	3.00	2.00	97	1.49	0.81	0.00	3.00	1.00
Cleared	84	1.86	0.87	0.00	3.00	2.00	97	1.59	0.73	0.00	3.00	1.00
Month 3	76	1.59	0.79	0.00	3.00	1.00	95	1.46	0.68	0.00	3.00	1.00
Month 6	73	1.58	0.83	0.00	3.00	1.00	94	1.46	0.65	0.00	3.00	1.00
Month 9	70	1.69	0.79	0.00	3.00	2.00	92	1.43	0.72	0.00	3.00	1.00
Month 12	68	1.59	0.85	0.00	3.00	1.00	90	1.50	0.75	0.00	3.00	1.00
Month 15	66	1.48	0.77	0.00	3.00	1.50	89	1.37	0.76	0.00	3.00	1.00
Month 18	65	1.40	0.75	0.00	3.00	1.00	88	1.28	0.73	0.00	3.00	1.00

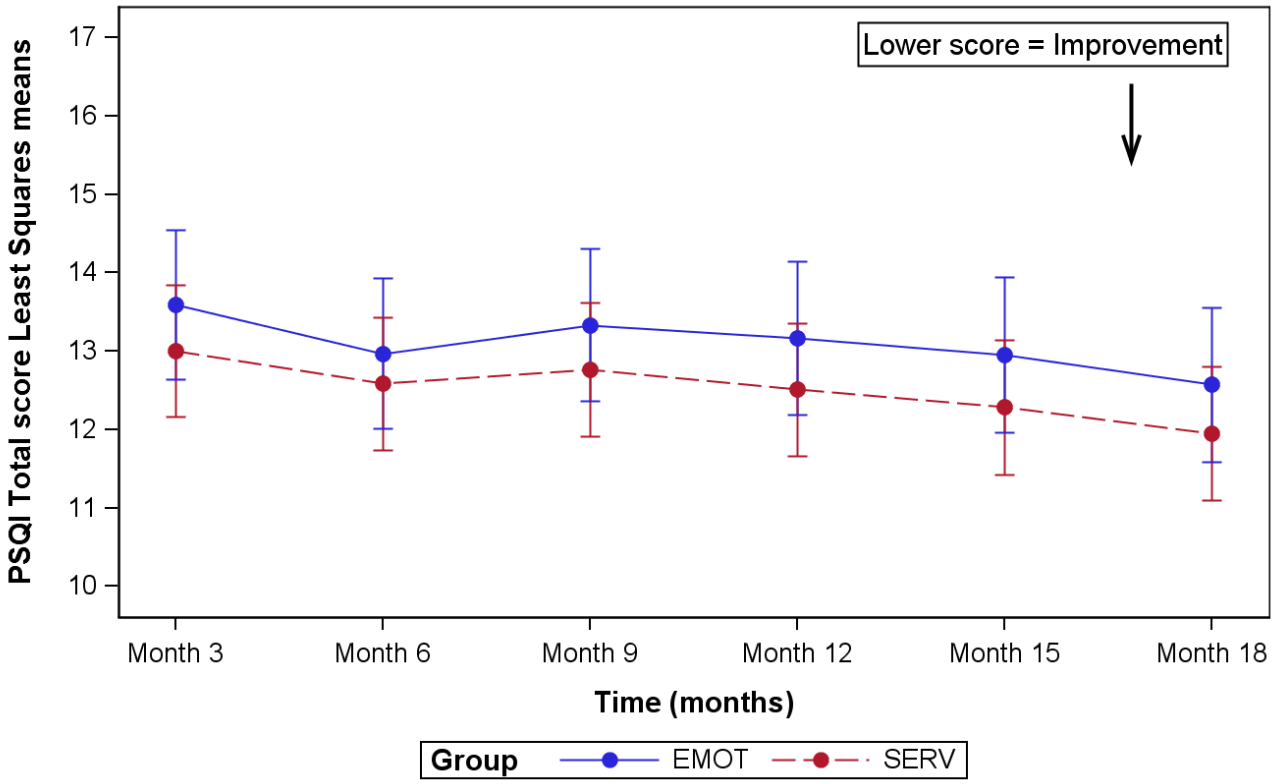
Table GGG. Random Intercept model results for the PSQI (PP)

		Random Int (PP)	
Outcome	**Effect**	**F statistic**	**P-value**
PSQI	Baseline score	99.50	<.0001
	Gender	1.29	0.2568
	Center	1.86	0.1589
	Treatment	1.46	0.2289
	Time	3.17	0.0077
	Treatment*Time	0.07	0.9964

Table HHH.1. Effect of SERV Intervention vs. EMOT Intervention for PSQI (PP)

	Outcome Measure	Population-Model Type	PP			
			Estimate	95% CI Lower	95% CI Upper	P-value
SERV vs. EMOT over time	PSQI	random intercept	-0.5815	-1.5321	0.3691	0.2289
SERV vs. EMOT at 18 months	PSQI	random intercept	-0.6246	-1.8277	0.5785	0.3080

Figure HHH.2. PSQI total score Least Squares Means and 95% confidence intervals over time by Treatment from the random intercept model (lower score=improvement; PP population)



Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

Table HHH.3. PSQI total score Least Squares Means (Adjusted) and 95% confidence intervals over time by Treatment from the random intercept model (lower score=improvement; PP population)

	EMOT		SERV	
Time	**N**	**Adjusted Mean (95% CI)**	**N**	**Adjusted Mean (95% CI)**
3	75	13.59 (12.64, 14.54)	95	13.01 (12.17, 13.84)
6	73	12.97 (12.01, 13.93)	94	12.58 (11.74, 13.42)
9	69	13.33 (12.36, 14.30)	91	12.76 (11.92, 13.61)
12	68	13.17 (12.19, 14.15)	90	12.51 (11.66, 13.36)
15	64	12.95 (11.96, 13.94)	88	12.28 (11.43, 13.14)
18	65	12.57 (11.58, 13.56)	87	11.95 (11.09, 12.80)

Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

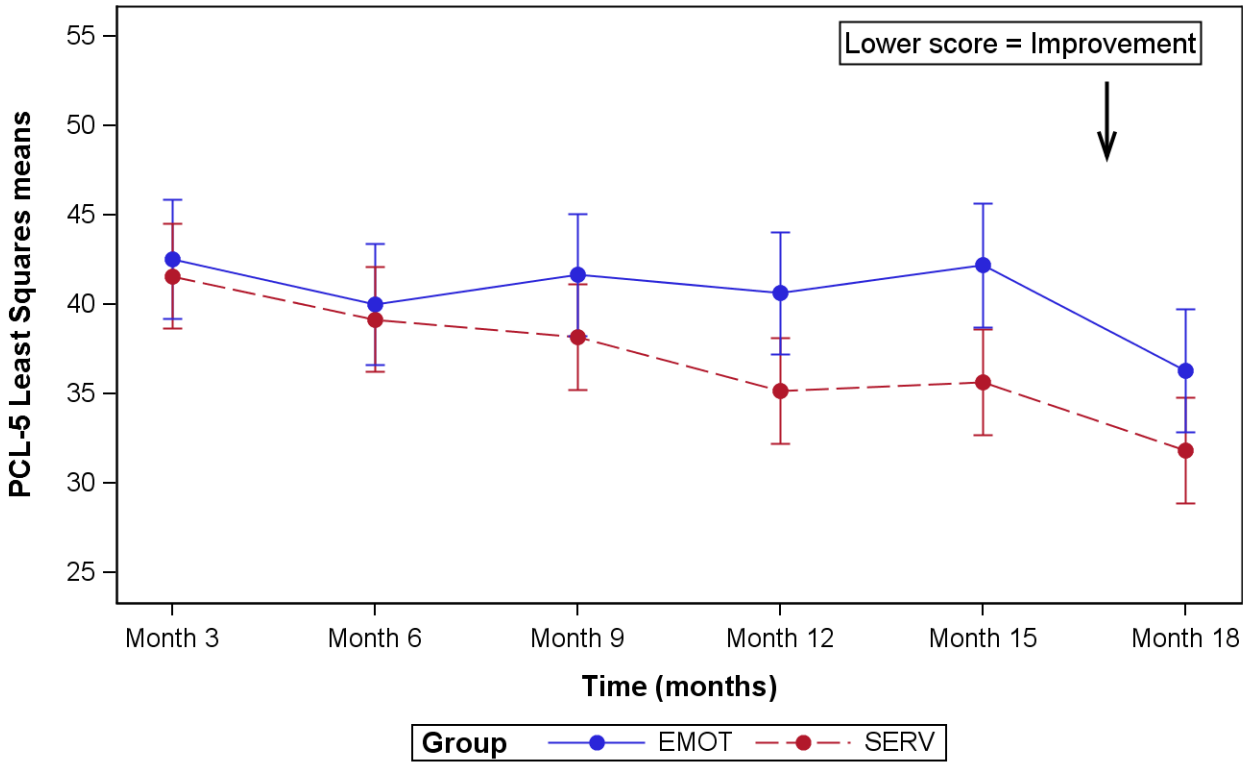
Table III. Random Intercept model results for the PCL-5 (PP)

		Random Int (PP)	
Outcome	**Effect**	**F statistic**	**P-value**
PCL-5	Baseline score	100.46	<.0001
	Gender	0.25	0.6187
	Center	3.58	0.0302
	Treatment	4.35	0.0385
	Time	16.58	<.0001
	Treatment*Time	3.27	0.0063

Table JJJ.1. Effect of SERV Intervention vs. EMOT Intervention for PCL-5 (PP)

	Outcome Measure	Population-Model Type	PP			
			Estimate	95% CI Lower	95% CI Upper	P-value
SERV vs. EMOT over time	PCL-5	random intercept	-3.6178	-7.0420	-0.1935	0.0385
SERV vs. EMOT at 18 months	PCL-5	random intercept	-4.4720	-8.6564	-0.2876	0.0363

Figure JJJ.2. PCL-5 score Least Squares Means and 95% confidence intervals over time by Treatment from the random intercept model (lower score=improvement; PP population)



Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

Table JJJ.3. PCL-5 score Least Squares Means (Adjusted) and 95% confidence intervals over time by Treatment from the random intercept model (lower score=improvement; PP population)

	EMOT		SERV	
Time	**N**	**Adjusted Mean (95% CI)**	**N**	**Adjusted Mean (95% CI)**
3	76	42.53 (39.18, 45.87)	95	41.58 (38.66, 44.51)
6	73	40.00 (36.63, 43.37)	94	39.17 (36.23, 42.11)
9	70	41.65 (38.25, 45.05)	92	38.19 (35.24, 41.14)
12	68	40.64 (37.21, 44.06)	90	35.18 (32.21, 38.14)
15	66	42.19 (38.75, 45.63)	89	35.65 (32.68, 38.62)
18	65	36.31 (32.85, 39.76)	88	31.83 (28.86, 34.81)

Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

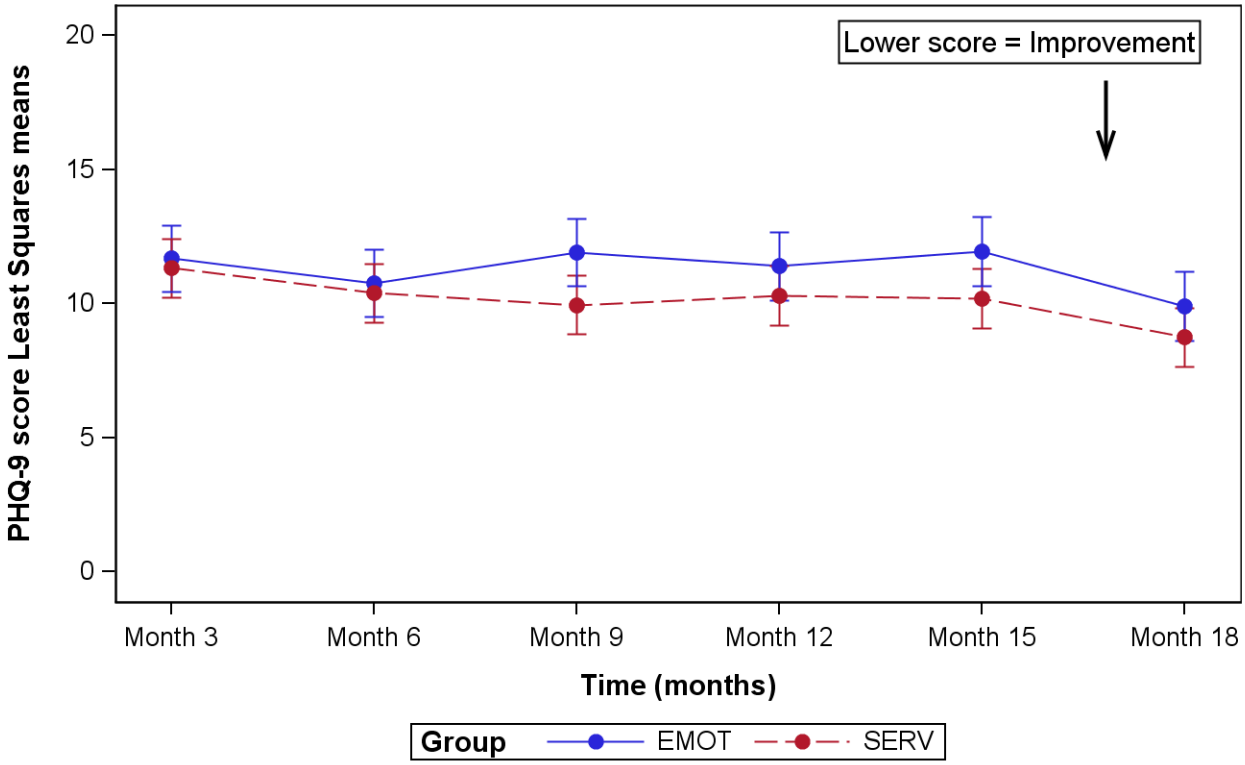
Table KKK. Random Intercept model results for the PHQ-9 (PP)

		Random Int (PP)	
Outcome	**Effect**	**F statistic**	**P-value**
PHQ-9	Baseline score	71.31	<.0001
	Gender	2.67	0.1040
	Center	5.55	0.0046
	Treatment	3.16	0.0775
	Time	8.27	<.0001
	Treatment*Time	1.78	0.1146

Table LLL.1. Effect of SERV Intervention vs. EMOT Intervention for PHQ-9 (PP)

	Outcome Measure	**Population -Model Type**	**PP**			
			Estimate	**95% CI Lower**	**95% CI Upper**	**P-value**
SERV vs. EMOT over time	PHQ-9	random intercept	-1.1221	-2.3691	0.1250	0.0775
SERV vs. EMOT at 18 months	PHQ-9	random intercept	-1.1746	-2.7391	0.3899	0.1407

Figure LLL.2. PHQ-9 score Least Squares Means and 95% confidence intervals over time by Treatment from the random intercept model (lower score=improvement; PP population)



Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

Table LLL.3. PHQ-9 score Least Squares Means (Adjusted) and 95% confidence intervals over time by Treatment from the random intercept model (lower score=improvement; PP population)

	EMOT		SERV	
Time	**N**	**Adjusted Mean (95% CI)**	**N**	**Adjusted Mean (95% CI)**
3	76	11.68 (10.44, 12.92)	95	11.32 (10.24, 12.41)
6	73	10.77 (9.52, 12.02)	94	10.40 (9.30, 11.49)
9	70	11.90 (10.64, 13.17)	92	9.94 (8.84, 11.04)
12	68	11.40 (10.12, 12.67)	90	10.30 (9.20, 11.40)
15	66	11.95 (10.67, 13.23)	88	10.18 (9.07, 11.28)
18	65	9.91 (8.63, 11.20)	88	8.74 (7.63, 9.84)

Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

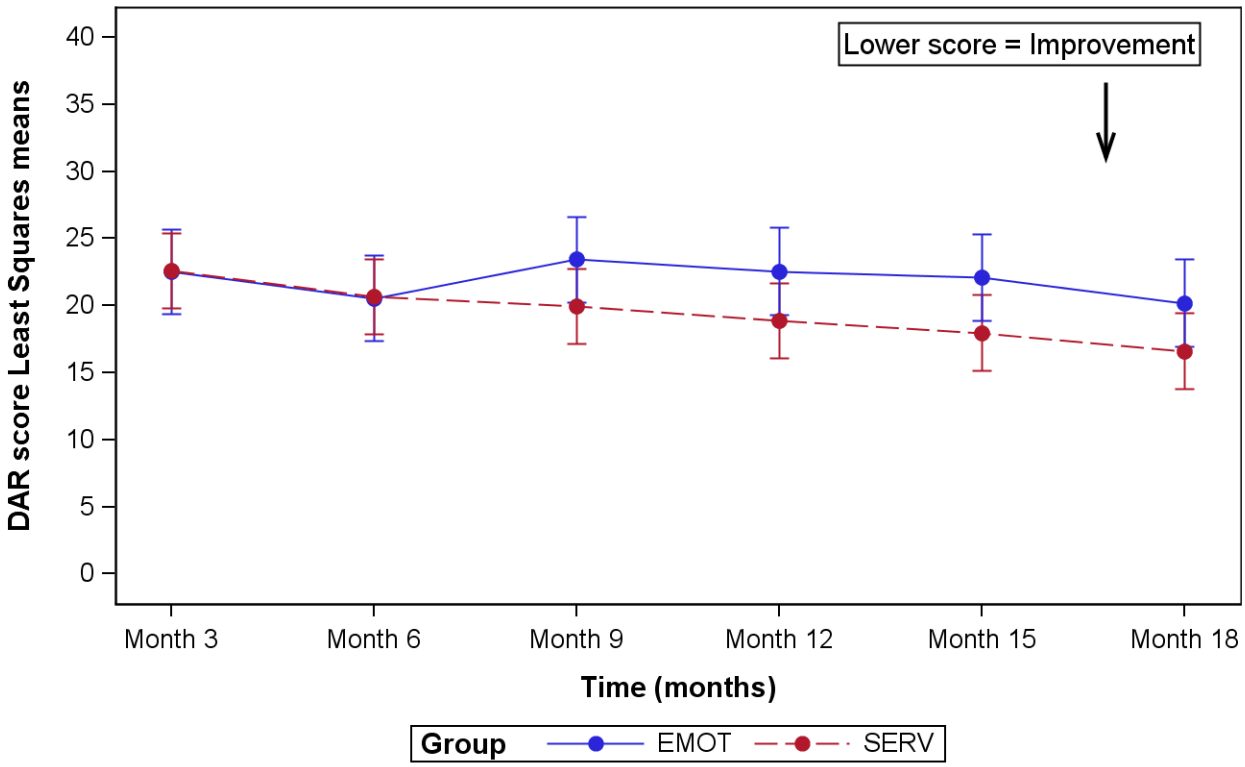
Table MMM. Random Intercept model results for the DAR (PP)

		Random Int (PP)	
Outcome	**Effect**	**F statistic**	**P-value**
DAR	Baseline score	86.37	<.0001
	Gender	0.21	0.6454
	Center	8.11	0.0004
	Treatment	2.08	0.1513
	Time	6.67	<.0001
	Treatment*Time	3.22	0.0069

Table NNN.1. Effect of SERV Intervention vs. EMOT Intervention for DAR (PP)

			PP			
	Outcome Measure	**Population-Model Type**	**Estimate**	**95% CI Lower**	**95% CI Upper**	**P-value**
SERV vs. EMOT over time	DAR	random intercept	-2.4427	-5.7878	0.9024	0.1513
SERV vs. EMOT at 18 months	DAR	random intercept	-3.5726	-7.4908	0.3457	0.0738

Figure NNN.2. DAR score Least Squares Means and 95% confidence intervals over time by Treatment from the random intercept model (lower score=improvement; PP population)



Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

Table NNN.3. DAR score Least Squares Means (Adjusted) and 95% confidence intervals over time by Treatment from the random intercept model (lower score=improvement; PP population)

	EMOT		SERV	
Time	**N**	**Adjusted Mean (95% CI)**	**N**	**Adjusted Mean (95% CI)**
3	76	22.52 (19.36, 25.69)	95	22.58 (19.80, 25.35)
6	73	20.52 (17.34, 23.71)	94	20.63 (17.85, 23.42)
9	70	23.42 (20.21, 26.63)	92	19.96 (17.16, 22.75)
12	68	22.56 (19.33, 25.78)	90	18.88 (16.08, 21.69)
15	66	22.08 (18.83, 25.32)	89	17.96 (15.15, 20.77)
18	65	20.17 (16.92, 23.42)	88	16.60 (13.78, 19.41)

Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

Table OOO. Unadjusted WHO-DAS 2.0 Overall Summary Score (lower score = less disability) over time by group (PPDR)

	EMOT						SERV					
Visits	**N**	**Mean**	**SD**	**Min**	**Max**	**Median**	**N**	**Mean**	**SD**	**Min**	**Max**	**Median**
Screened	83	40.41	15.93	6	92	38	97	37.75	16.65	5	84	36
Cleared	84	45.55	17.84	3	91	47	97	43.52	16.94	1	76	43
Month 3	70	42.23	16.96	2	76	43.5	95	39.95	16.21	5	83	39
Month 6	67	42.22	17.12	1	95	45	94	37.90	15.88	7	80	38.5
Month 9	64	43.72	18.62	2	95	42	91	37.68	17.20	0	80	36
Month 12	63	41.41	17.47	1	91	42	88	37.00	16.70	0	79	35.5
Month 15	61	43.07	17.63	0	92	43	85	36.40	17.53	0	85	35
Month 18	60	38.45	17.50	0	69	39	85	33.49	17.13	2	88	32

Table PPP. Unadjusted WHO-DAS 2.0 Domain Scores (lower score = less disability) over time by group (PPDR)

Cognition

	EMOT						SERV					
Visits	**N**	**Mean**	**SD**	**Min**	**Max**	**Median**	**N**	**Mean**	**SD**	**Min**	**Max**	**Median**
Baseline	84	36.25	18.08	0	95	35	97	35.98	20.20	0	100	35
Cleared	84	43.87	18.94	0	90	45	97	41.39	19.43	0	90	45
Month 3	70	40.86	17.34	0	70	40	95	38.16	17.31	0	80	40
Month 6	67	39.40	18.21	0	90	40	94	36.01	16.65	5	70	35
Month 9	64	41.88	19.85	0	100	40	91	36.46	18.33	0	80	35
Month 12	63	38.51	18.04	0	85	40	88	34.88	18.70	0	80	30
Month 15	61	39.75	19.31	0	90	40	86	33.26	19.51	0	80	30
Month 18	60	35.00	18.43	0	70	35	85	31.82	17.16	0	80	30

Mobility

	EMOT						SERV					
Visits	**N**	**Mean**	**SD**	**Min**	**Max**	**Median**	**N**	**Mean**	**SD**	**Min**	**Max**	**Median**
Baseline	84	30.98	23.27	0	87.5	28.15	97	25.60	22.81	0	93.8	18.8
Cleared	84	39.90	22.00	0	93.8	43.8	97	34.63	23.18	0	93.8	37.5
Month 3	70	36.36	22.66	0	87.5	37.5	95	33.23	23.02	0	81.3	31.3
Month 6	67	40.32	24.63	0	100	43.8	94	35.06	25.18	0	93.8	37.5
Month 9	64	40.85	24.76	0	100	43.8	91	34.57	24.25	0	100	37.5
Month 12	63	38.52	24.13	0	87.5	43.8	88	33.92	24.07	0	100	31.3
Month 15	61	42.65	25.99	0	100	43.8	86	32.72	24.96	0	87.5	31.3
Month 18	60	36.69	23.01	0	81.3	37.5	85	31.05	24.35	0	87.5	31.3

Self-Care

	EMOT						SERV					
Visits	**N**	**Mean**	**SD**	**Min**	**Max**	**Median**	**N**	**Mean**	**SD**	**Min**	**Max**	**Median**
Baseline	84	14.76	18.98	0	80	10	97	13.51	18.03	0	60	10
Cleared	84	19.76	20.59	0	90	10	97	20.00	20.67	0	80	10
Month 3	70	20.14	20.54	0	80	10	95	17.68	19.32	0	70	10
Month 6	67	20.45	20.70	0	80	20	94	16.49	18.65	0	80	10
Month 9	64	24.06	22.16	0	100	20	91	17.69	20.71	0	70	10
Month 12	63	20.05	20.24	0	80	20	88	18.41	19.70	0	70	10
Month 15	61	22.35	20.69	0	60	20	86	16.74	18.94	0	70	10
Month 18	60	19.17	19.16	0	60	10	85	15.76	18.02	0	60	10

Interpersonal Interactions

	EMOT						SERV					
Visits	**N**	**Mean**	**SD**	**Min**	**Max**	**Median**	**N**	**Mean**	**SD**	**Min**	**Max**	**Median**
Baseline	83	50.86	23.40	0	100	50	97	51.81	22.58	0	100	50
Cleared	84	56.45	23.97	0	100	58.3	97	56.76	23.63	0	100	58.3
Month 3	70	51.19	22.40	0	100	50	95	53.16	21.31	0	100	50
Month 6	67	50.74	22.23	0	100	50	94	46.37	22.52	0	100	45.85
Month 9	64	50.72	23.78	0	100	50	91	48.45	19.92	0	100	50
Month 12	63	47.09	23.26	0	100	50	88	45.60	21.35	0	91.7	41.7
Month 15	61	53.18	23.83	0	100	50	86	48.67	20.57	0	100	45.85
Month 18	60	47.71	25.60	0	100	50	85	41.16	22.73	0	100	41.7

Life Activities – Domestic

	EMOT						SERV					
Visits	**N**	**Mean**	**SD**	**Min**	**Max**	**Median**	**N**	**Mean**	**SD**	**Min**	**Max**	**Median**
Baseline	84	39.88	24.71	0	100	40	97	35.26	25.00	0	100	40
Cleared	84	46.90	27.33	0	100	50	97	44.74	25.25	0	100	50
Month 3	70	47.43	24.71	0	100	50	95	41.05	26.84	0	100	40
Month 6	67	45.97	23.94	0	100	50	94	41.38	25.34	0	100	40
Month 9	64	47.92	24.72	0	100	45	91	42.31	23.67	0	100	40
Month 12	63	47.78	25.49	0	100	50	88	41.78	22.69	0	100	40
Month 15	61	49.18	26.54	0	100	50	85	40.12	26.97	0	100	40
Month 18	60	45.00	24.46	0	100	40	85	37.18	24.67	0	100	40

Life Activities – Work, School

	EMOT						SERV					
Visits	**N**	**Mean**	**SD**	**Min**	**Max**	**Median**	**N**	**Mean**	**SD**	**Min**	**Max**	**Median**
Baseline	42	37.08	18.55	0	78.6	35.7	53	34.51	29.21	0	100	28.6
Cleared	46	48.29	25.25	0	100	50	47	39.57	20.84	0	92.9	42.9
Month 3	38	46.25	22.81	0	100	42.9	45	35.88	23.32	0	92.9	35.7
Month 6	30	41.91	24.73	0	100	42.9	40	28.40	21.50	0	78.6	28.6
Month 9	29	46.89	26.28	0	100	42.9	38	28.20	21.97	0	85.7	28.6
Month 12	28	39.54	23.12	0	100	35.7	45	34.82	23.43	0	85.7	28.6
Month 15	32	45.24	22.84	0	100	42.9	42	34.01	21.74	0	71.4	35.7
Month 18	28	35.45	21.60	0	85.7	32.15	46	32.92	21.00	0	78.6	32.15

Participation in Society

	EMOT						SERV					
Visits	**N**	**Mean**	**SD**	**Min**	**Max**	**Median**	**N**	**Mean**	**SD**	**Min**	**Max**	**Median**
Baseline	84	56.49	19.55	0	100	56.25	97	51.98	19.71	8.3	91.7	50
Cleared	84	55.46	20.94	4.2	95.8	54.2	97	54.51	19.85	4.2	95.8	58.3
Month 3	70	49.28	19.96	0	87.5	47.9	95	48.37	19.41	0	100	45.8
Month 6	67	49.25	19.81	0	100	50	94	45.76	18.50	0	95.8	45.8
Month 9	64	49.48	19.56	4.2	100	50	91	43.09	19.66	0	100	45.8
Month 12	63	49.41	19.77	4.2	100	50	88	42.75	18.28	0	83.3	41.7
Month 15	61	47.23	20.25	0	95.8	45.8	86	42.11	19.82	0	100	39.9
Month 18	60	43.76	20.72	0	87.5	41.7	85	38.72	19.97	4.2	100	33.3

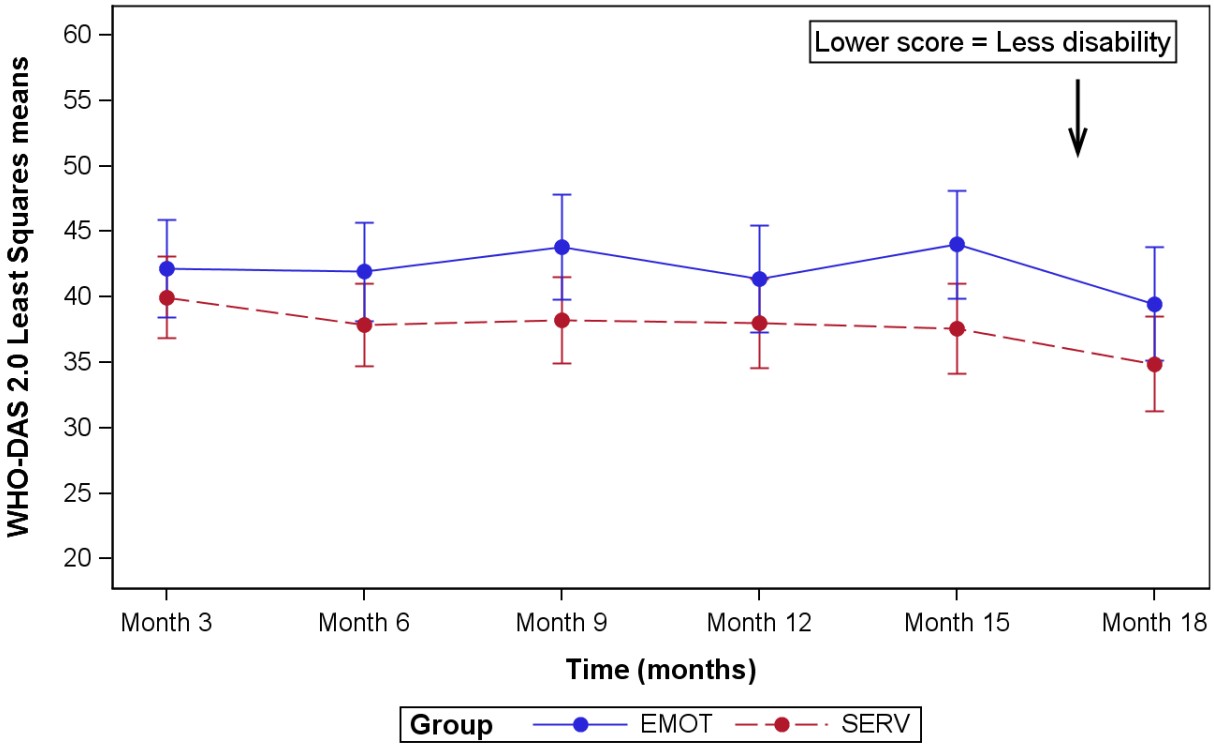
Table QQQ. Linear Mixed Repeated Measures model and Random Intercept model results for WHO-DAS 2.0 (PPDR)

		Repeated (PPDR)		Random Int (PPDR)	
Outcome	**Effect**	**F statistic**	**P-value**	**F statistic**	**P-value**
WHO-DAS 2.0	Baseline score	73.50	<.0001	62.34	<.0001
	Gender	3.41	0.0665	2.24	0.1365
	Center	6.61	0.0017	7.12	0.0011
	Treatment	4.44	0.0368	4.53	0.0348
	Time	4.76	0.0005	5.12	0.0001
	Treatment*Time	1.22	0.3006	1.36	0.2384

Table RRR.1 Effect of SERV Intervention vs. EMOT Intervention for WHO-DAS 2.0 (PPDR)

	Outcome Measure	Population-Model Type	PPDR			
			Estimate	**95% CI Lower**	**95% CI Upper**	**P-value**
SERV vs. EMOT over time	WHO-DAS 2.0	repeated	-4.3731	-8.4737	-0.2725	0.0368
SERV vs. EMOT at 18 months	WHO-DAS 2.0	repeated	-4.5669	-9.7765	0.6427	0.0853
SERV vs. EMOT over time	WHO-DAS 2.0	random intercept	-4.3816	-8.4457	-0.3174	0.0348
SERV vs. EMOT at 18 months	WHO-DAS 2.0	random intercept	-4.4803	-9.2252	0.2646	0.0641

Figure RRR.2. WHO-DAS 2.0 overall summary score Least Squares Means and 95% confidence intervals over time by Treatment from the linear mixed repeated measures model (lower score=improvement; PPDR population)



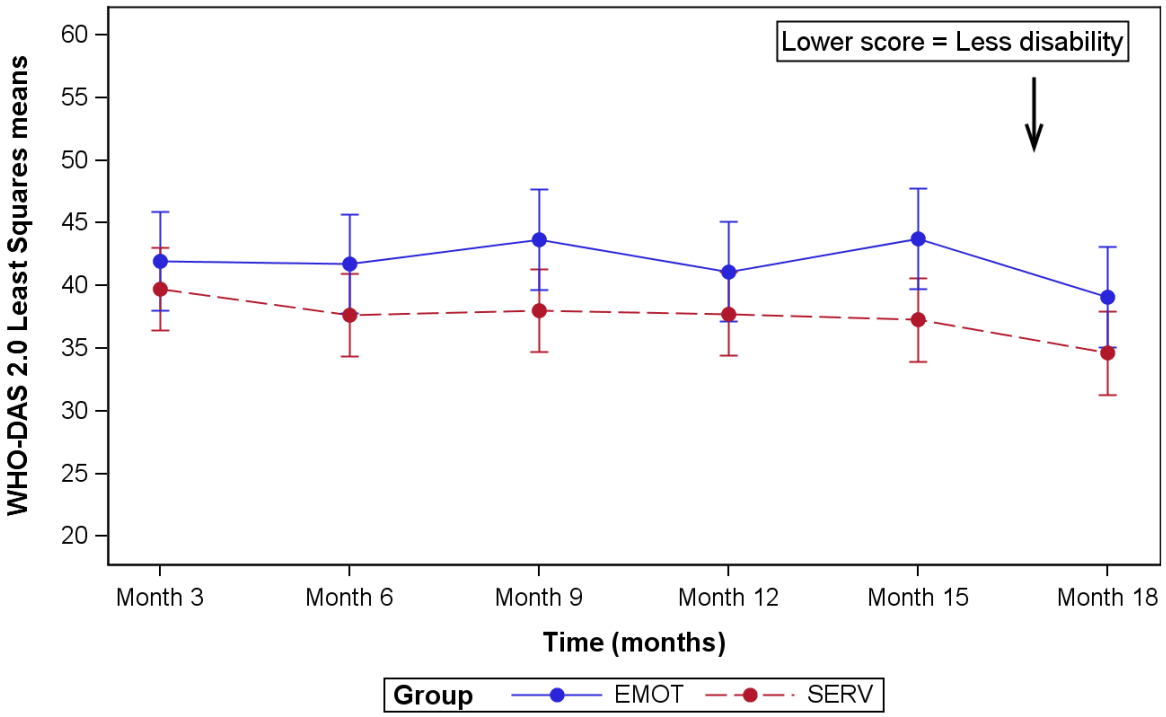
Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

Table RRR.3. WHO-DAS 2.0 overall summary score Least Squares Means (Adjusted) and 95% confidence intervals over time by Treatment from the linear mixed repeated measures model (lower score=improvement; PPDR population)

	EMOT		SERV	
Time	**N**	**Adjusted Mean (95% CI)**	**N**	**Adjusted Mean (95% CI)**
3	70	42.17 (38.46, 45.89)	95	39.96 (36.86, 43.06)
6	67	41.94 (38.18, 45.70)	94	37.85 (34.72, 40.98)
9	64	43.81 (39.83, 47.80)	91	38.24 (34.94, 41.55)
12	63	41.37 (37.28, 45.45)	88	37.99 (34.59, 41.39)
15	61	43.99 (39.90, 48.08)	85	37.57 (34.15, 40.98)
18	60	39.45 (35.12, 43.79)	85	34.89 (31.27, 38.50)

Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

Figure RRR.4. WHO-DAS 2.0 overall summary score Least Squares Means and 95% confidence intervals over time by Treatment from the random intercept model (lower score=improvement; PPDR population)



Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

Table RRR.5. WHO-DAS 2.0 overall summary score Least Squares Means (Adjusted) and 95% confidence intervals over time by Treatment from the random intercept model (lower score=improvement; PPDR population)

	EMOT		SERV	
Time	**N**	**Adjusted Mean (95% CI)**	**N**	**Adjusted Mean (95% CI)**
3	70	41.95 (38.03, 45.87)	95	39.73 (36.45, 43.01)
6	67	41.73 (37.77, 45.68)	94	37.63 (34.34, 40.92)
9	64	43.66 (39.68, 47.64)	91	38.02 (34.71, 41.32)
12	63	41.12 (37.13, 45.11)	88	37.74 (34.41, 41.06)
15	61	43.74 (39.73, 47.75)	85	37.28 (33.94, 40.62)
18	60	39.09 (35.07, 43.11)	85	34.61 (31.27, 37.95)

Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

Table SSS. Unadjusted VR-12 PCS and MCS (higher score = better) over time by group (PPDR)

		EMOT						SERV					
	Visits	n	Mean	SD	Min	Max	Median	n	Mean	SD	Min	Max	Median
PCS	Baseline	83	40.16	9.94	22.47	60.49	39.11	97	43.07	11.20	22.80	69.33	41.82
	Cleared	82	38.70	11.53	18.49	62.72	36.27	97	40.76	10.90	17.43	65.34	39.30
	Month 3	69	37.12	11.00	17.12	64.72	34.29	94	39.05	11.08	21.60	64.90	37.41
	Month 6	65	36.14	11.00	16.45	59.99	33.54	94	39.80	11.59	17.10	64.46	38.28
	Month 9	63	35.66	11.68	16.87	62.95	34.09	88	39.19	11.67	19.28	66.51	38.60
	Month 12	63	36.15	12.50	15.28	59.86	33.71	87	39.14	11.40	17.09	61.62	38.39
	Month 15	61	36.10	11.69	15.98	62.44	34.94	84	39.69	11.53	13.27	63.11	39.53
	Month 18	58	37.64	11.87	11.93	64.20	38.52	84	38.88	11.64	9.09	61.81	38.19
MCS	Baseline	83	31.11	10.62	13.67	59.63	29.89	97	30.68	10.37	11.71	59.33	29.79
	Cleared	82	31.14	11.04	11.18	63.80	30.59	97	30.57	10.49	7.32	63.26	30.36
	Month 3	69	35.85	10.62	12.16	61.00	35.47	94	35.81	9.07	15.00	55.97	36.12
	Month 6	65	36.66	11.64	12.27	61.85	35.89	94	35.71	8.91	17.31	55.54	35.99
	Month 9	63	34.52	10.53	12.11	60.99	33.47	88	36.33	9.96	14.27	54.65	37.20
	Month 12	63	37.31	10.91	19.54	63.84	35.87	87	37.01	10.93	14.65	60.98	38.20
	Month 15	61	36.90	10.38	19.16	60.26	36.02	84	37.78	11.46	13.46	62.93	39.00
	Month 18	58	39.36	12.23	12.37	60.26	39.04	84	40.54	9.30	19.33	56.48	41.30

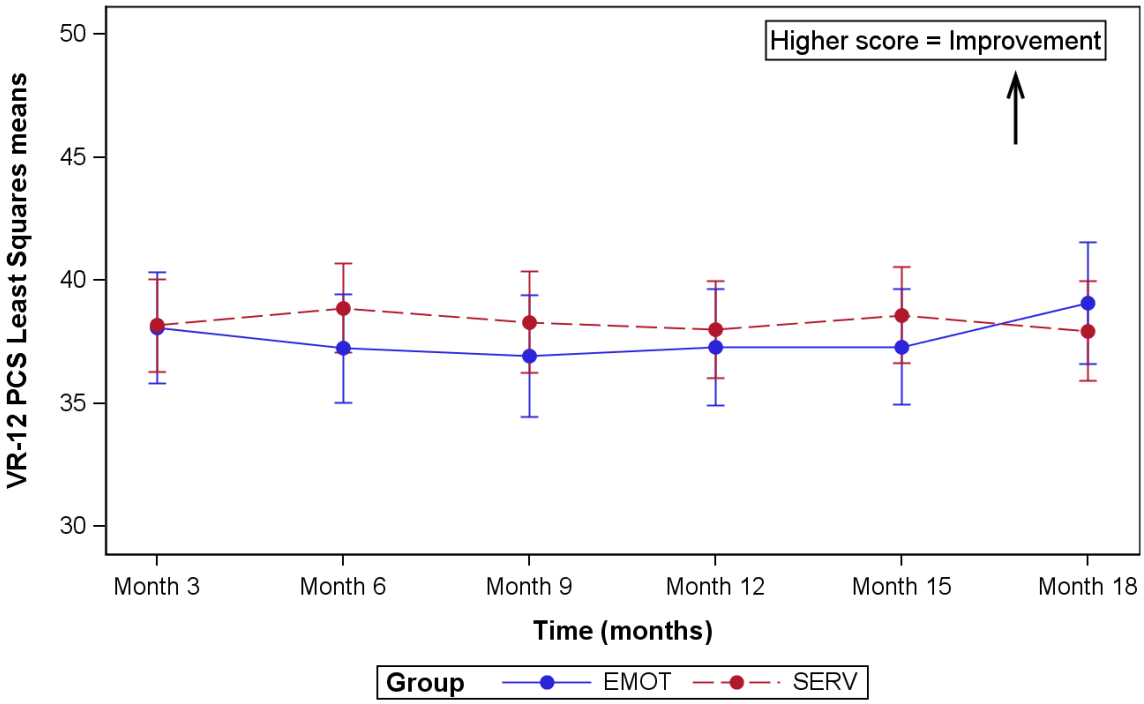
Table TTT. Linear Mixed Repeated Measures model and Random Intercept model results for the VR-12 PCS and MCS (PPDR)

		Repeated (PPDR)		Random Int (PPDR)	
Outcome	Effect	F statistic	P-value	F statistic	P-value
VR-12 PCS	Baseline score	163.67	<.0001	161.17	<.0001
	Gender	0.08	0.7838	0.26	0.6094
	Center	0.23	0.7924	0.39	0.6754
	Treatment	0.31	0.5776	0.38	0.5378
	Time	0.51	0.7682	0.67	0.6443
	Treatment*Time	1.20	0.3130	1.52	0.1811
VR-12 MCS	Baseline score	63.81	<.0001	68.63	<.0001
	Gender	6.43	0.0122	5.01	0.0265
	Center	3.20	0.0433	4.32	0.0150
	Treatment	0.59	0.4446	0.54	0.4644
	Time	5.93	<.0001	7.03	<.0001
	Treatment*Time	1.46	0.2062	1.21	0.3006

Table UUU.1. Effect of SERV Intervention vs. EMOT Intervention for VR-12 PCS and MCS (PPDR)

	Outcome Measure	Population-Model Type	PPDR			
			Estimate	95% CI Lower	95% CI Upper	P-value
SERV vs. EMOT over time	VR-12 PCS	repeated	0.6584	-1.6718	2.9886	0.5776
SERV vs. EMOT at 18 months	VR-12 PCS	repeated	-1.1434	-4.1105	1.8237	0.4477
SERV vs. EMOT over time	VR-12 PCS	random intercept	0.7262	-1.5962	3.0486	0.5378
SERV vs. EMOT at 18 months	VR-12 PCS	random intercept	-1.1693	-4.0026	1.6641	0.4175
SERV vs. EMOT over time	VR-12 MCS	repeated	0.8873	-1.3995	3.1741	0.4446
SERV vs. EMOT at 18 months	VR-12 MCS	repeated	1.7179	-1.4900	4.9257	0.2917
SERV vs. EMOT over time	VR-12 MCS	random intercept	0.8416	-1.4249	3.1080	0.4644
SERV vs. EMOT at 18 months	VR-12 MCS	random intercept	1.7521	-1.2990	4.8031	0.2597

Figure UUU.2. VR-12 PCS summary score Least Squares Means and 95% confidence intervals over time by Treatment from the linear mixed repeated measures model (higher score=improvement; PPDR population)



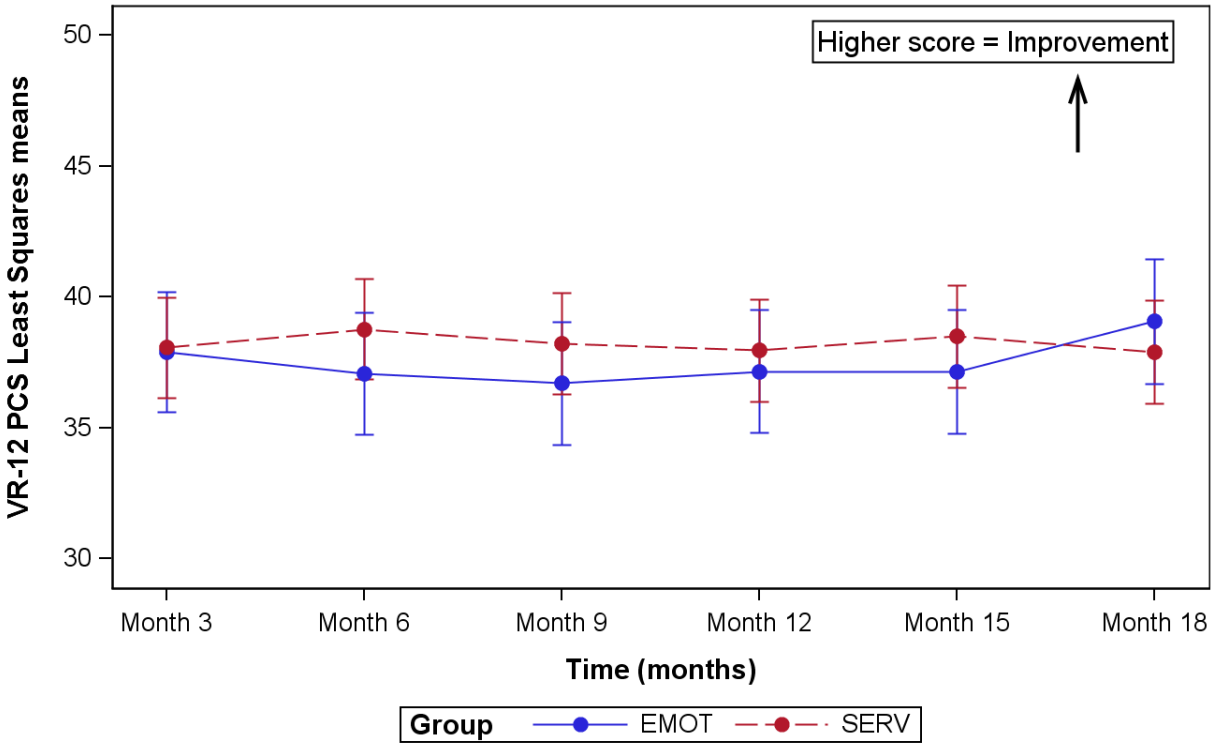
Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

Table UUU.3. VR-12 PCS summary score Least Squares Means (Adjusted) and 95% confidence intervals over time by Treatment from the linear mixed repeated measures model (higher score=improvement; PPDR population)

	EMOT		SERV	
Time	**N**	**Adjusted Mean (95% CI)**	**N**	**Adjusted Mean (95% CI)**
3	69	38.08 (35.83, 40.34)	94	38.17 (36.29, 40.05)
6	65	37.24 (35.04, 39.45)	94	38.87 (37.05, 40.68)
9	63	36.93 (34.46, 39.40)	88	38.30 (36.25, 40.36)
12	63	37.28 (34.92, 39.65)	87	38.01 (36.04, 39.98)
15	61	37.30 (34.96, 39.64)	84	38.58 (36.64, 40.53)
18	58	39.09 (36.62, 41.56)	84	37.94 (35.91, 39.98)

Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

Figure UUU.4. VR-12 PCS summary score Least Squares Means and 95% confidence intervals over time by Treatment from the random intercept model (higher score=improvement; PPDR population)



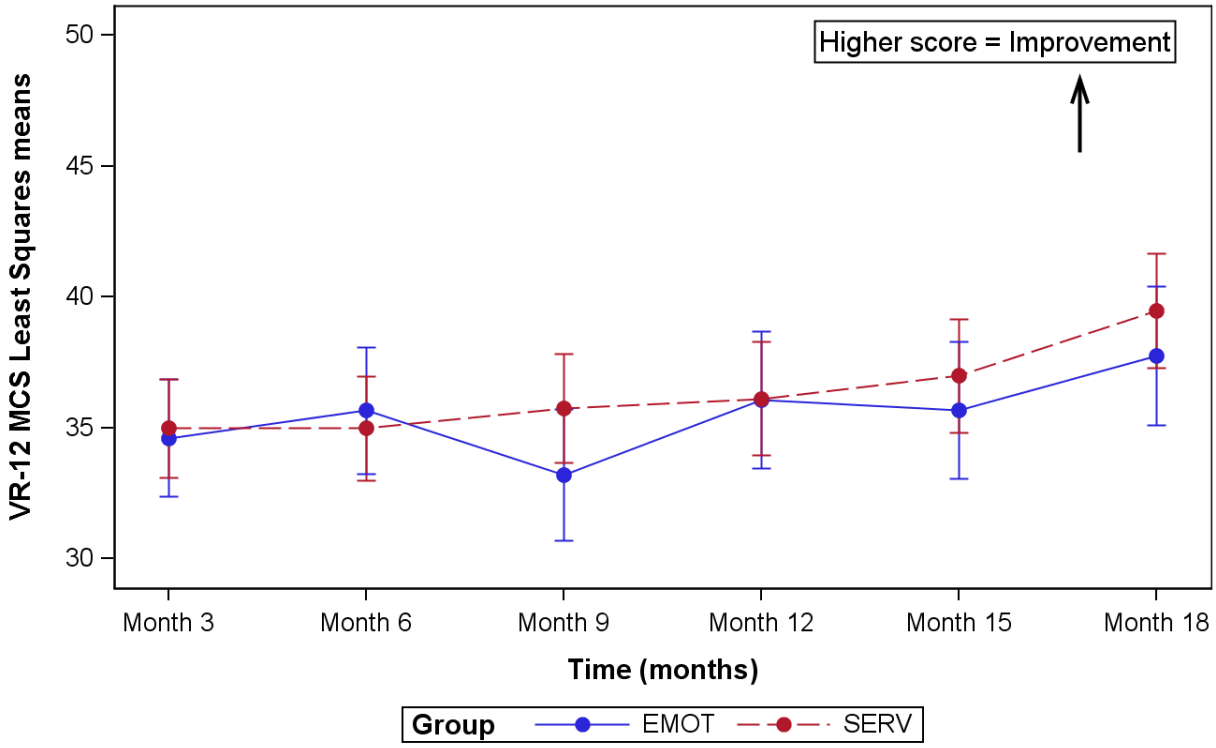
Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

Table UUU.5. VR-12 PCS summary score Least Squares Means (Adjusted) and 95% confidence intervals over time by Treatment from the random intercept model (higher score=improvement; PPDR population)

	EMOT		SERV	
Time	**N**	**Adjusted Mean (95% CI)**	**N**	**Adjusted Mean (95% CI)**
3	69	37.90 (35.60, 40.20)	94	38.07 (36.15, 39.98)
6	65	37.06 (34.74, 39.39)	94	38.76 (36.84, 40.68)
9	63	36.71 (34.36, 39.05)	88	38.21 (36.27, 40.15)
12	63	37.16 (34.81, 39.50)	87	37.96 (36.01, 39.91)
15	61	37.13 (34.78, 39.49)	84	38.49 (36.53, 40.45)
18	58	39.06 (36.68, 41.44)	84	37.89 (35.93, 39.85)

Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

Figure UUU.6. VR-12 MCS summary score Least Squares Means and 95% confidence intervals over time by Treatment from the linear mixed repeated measures model (higher score=improvement; PPDR population)



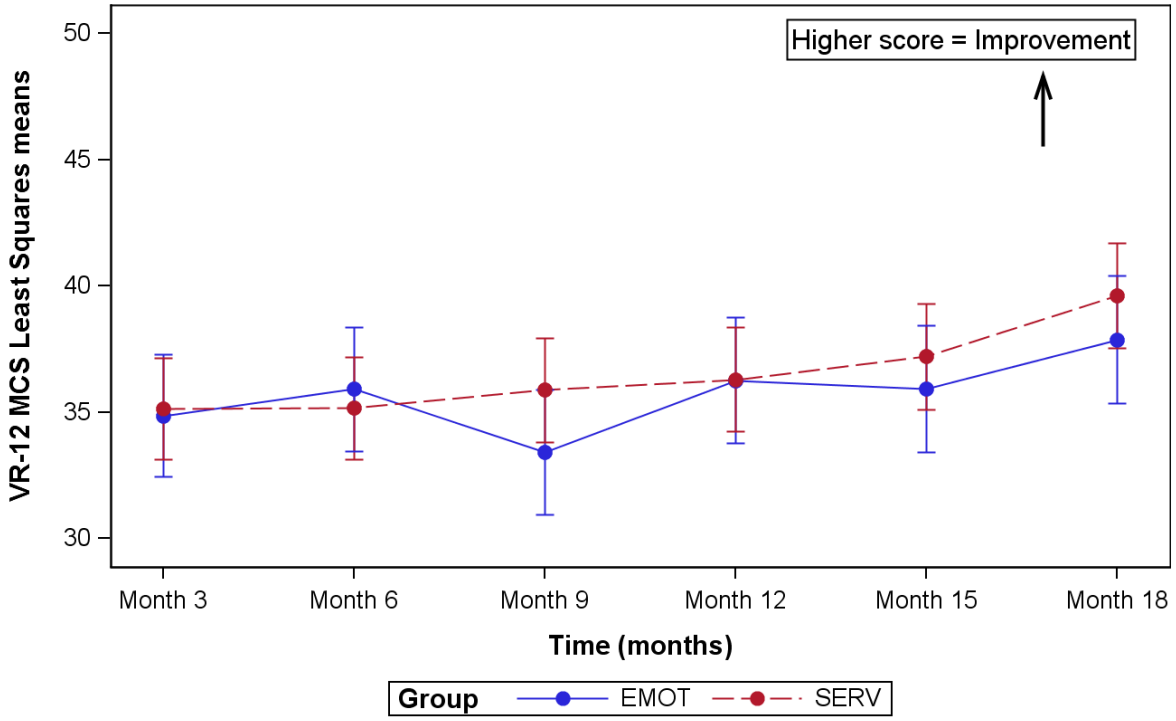
Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

Table UUU.7. VR-12 MCS summary score Least Squares Means (Adjusted) and 95% confidence intervals over time by Treatment from the linear mixed repeated measures model (higher score=improvement; PPDR population)

	EMOT		SERV	
Time	**N**	**Adjusted Mean (95% CI)**	**N**	**Adjusted Mean (95% CI)**
3	69	34.61 (32.36, 36.86)	94	34.98 (33.11, 36.85)
6	65	35.66 (33.25, 38.07)	94	34.98 (32.99, 36.96)
9	63	33.20 (30.70, 35.71)	88	35.74 (33.67, 37.82)
12	63	36.07 (33.45, 38.68)	87	36.12 (33.94, 38.29)
15	61	35.66 (33.06, 38.27)	84	36.99 (34.82, 39.16)
18	58	37.75 (35.10, 40.40)	84	39.47 (37.30, 41.65)

Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

Figure UUU.8. VR-12 MCS summary score Least Squares Means and 95% confidence intervals over time by Treatment from the random intercept model (higher score=improvement; PPDR population)



Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

Table UUU.9. VR-12 MCS summary score Least Squares Means (Adjusted) and 95% confidence intervals over time by Treatment from the random intercept model (higher score=improvement; PPDR population)

	EMOT		SERV	
Time	**N**	**Adjusted Mean (95% CI)**	**N**	**Adjusted Mean (95% CI)**
3	69	34.85 (32.43, 37.27)	94	35.13 (33.11, 37.15)
6	65	35.91 (33.45, 38.36)	94	35.16 (33.13, 37.18)
9	63	33.41 (30.93, 35.90)	88	35.87 (33.81, 37.93)
12	63	36.26 (33.78, 38.74)	87	36.30 (34.23, 38.36)
15	61	35.92 (33.42, 38.42)	84	37.20 (35.12, 39.28)
18	58	37.87 (35.34, 40.40)	84	39.62 (37.54, 41.70)

Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

Table VVV. Unadjusted PSQI Total Score (lower score = better) over time by group (PPDR)

	EMOT						SERV					
Visits	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**
Baseline	84	14.26	4.09	3.00	21.00	15.00	96	13.60	3.85	2.00	20.00	14.00
Cleared	83	14.63	4.10	3.00	21.00	15.00	97	13.76	4.17	3.00	21.00	15.00
Month 3	69	13.54	4.83	1.00	20.00	15.00	95	12.51	4.24	4.00	21.00	13.00
Month 6	67	13.09	4.70	1.00	21.00	13.00	94	12.17	4.13	4.00	21.00	12.50
Month 9	63	13.44	4.67	2.00	21.00	14.00	90	12.30	4.35	3.00	21.00	12.50
Month 12	63	13.25	5.01	2.00	21.00	15.00	88	12.10	4.25	4.00	21.00	12.50
Month 15	59	12.98	4.79	1.00	20.00	14.00	85	12.05	4.56	3.00	21.00	13.00
Month 18	60	12.43	4.94	2.00	20.00	14.00	85	11.59	4.27	2.00	21.00	12.00

Table WWW. Unadjusted PSQI Components (lower score = better) over time by group (PPDR)

Sleep Quality

	EMOT						SERV					
Visits	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**
Baseline	84	2.21	0.76	0.00	3.00	2.00	97	2.04	0.71	1.00	3.00	2.00
Cleared	84	2.06	0.83	0.00	3.00	2.00	97	2.07	0.74	1.00	3.00	2.00
Month 3	70	1.91	0.99	0.00	3.00	2.00	95	1.74	0.81	0.00	3.00	2.00
Month 6	67	1.88	0.83	0.00	3.00	2.00	94	1.70	0.72	1.00	3.00	2.00
Month 9	64	1.81	0.92	0.00	3.00	2.00	91	1.73	0.80	0.00	3.00	2.00
Month 12	63	1.90	0.89	0.00	3.00	2.00	88	1.69	0.70	1.00	3.00	2.00
Month 15	61	1.79	0.91	0.00	3.00	2.00	86	1.73	0.73	1.00	3.00	2.00
Month 18	60	1.73	0.78	0.00	3.00	2.00	86	1.57	0.82	0.00	3.00	1.00

Sleep Latency

	EMOT						SERV					
Visits	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**
Baseline	84	2.24	0.96	0.00	3.00	3.00	96	2.26	0.91	0.00	3.00	3.00
Cleared	83	2.42	0.84	0.00	3.00	3.00	97	2.37	0.83	0.00	3.00	3.00
Month 3	70	2.30	0.87	0.00	3.00	3.00	95	2.01	1.07	0.00	3.00	2.00
Month 6	67	2.24	0.91	0.00	3.00	3.00	94	2.07	0.92	0.00	3.00	2.00
Month 9	64	2.22	0.88	0.00	3.00	2.00	91	1.99	1.01	0.00	3.00	2.00
Month 12	63	2.19	0.95	0.00	3.00	2.00	88	2.00	1.08	0.00	3.00	2.00
Month 15	60	2.13	0.98	0.00	3.00	2.00	86	2.06	1.01	0.00	3.00	2.00
Month 18	60	1.98	1.05	0.00	3.00	2.00	86	1.94	1.02	0.00	3.00	2.00

Sleep Duration

	EMOT						SERV					
Visits	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**
Baseline	84	2.00	1.06	0.00	3.00	2.00	97	1.80	1.11	0.00	3.00	2.00
Cleared	84	1.79	1.18	0.00	3.00	2.00	97	1.75	1.12	0.00	3.00	2.00
Month 3	70	1.71	1.19	0.00	3.00	2.00	95	1.54	1.16	0.00	3.00	2.00
Month 6	67	1.60	1.24	0.00	3.00	2.00	94	1.45	1.13	0.00	3.00	1.00
Month 9	64	1.72	1.16	0.00	3.00	2.00	91	1.62	1.13	0.00	3.00	2.00
Month 12	63	1.75	1.16	0.00	3.00	2.00	88	1.63	1.20	0.00	3.00	2.00
Month 15	61	1.70	1.13	0.00	3.00	2.00	86	1.55	1.12	0.00	3.00	2.00
Month 18	60	1.45	1.14	0.00	3.00	2.00	86	1.53	1.12	0.00	3.00	1.50

Habitual Sleep Efficiency

	EMOT						SERV					
Visits	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**
Baseline	84	1.85	1.25	0.00	3.00	2.00	96	1.81	1.27	0.00	3.00	2.00
Cleared	84	2.02	1.13	0.00	3.00	2.00	97	1.72	1.25	0.00	3.00	2.00
Month 3	70	1.90	1.17	0.00	3.00	2.00	95	1.77	1.21	0.00	3.00	2.00
Month 6	67	1.66	1.21	0.00	3.00	2.00	94	1.61	1.20	0.00	3.00	1.50
Month 9	64	1.73	1.28	0.00	3.00	2.00	91	1.65	1.21	0.00	3.00	2.00
Month 12	63	1.75	1.22	0.00	3.00	2.00	88	1.65	1.21	0.00	3.00	2.00
Month 15	61	1.85	1.25	0.00	3.00	2.00	86	1.69	1.28	0.00	3.00	1.50
Month 18	60	1.82	1.13	0.00	3.00	2.00	86	1.57	1.26	0.00	3.00	1.00

Sleep Disturbance

	EMOT						SERV					
Visits	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**
Baseline	84	2.37	0.67	1.00	3.00	2.00	96	2.30	0.65	1.00	3.00	2.00
Cleared	83	2.43	0.63	1.00	3.00	3.00	97	2.34	0.68	1.00	3.00	2.00
Month 3	69	2.41	0.75	0.00	3.00	3.00	95	2.15	0.70	1.00	3.00	2.00
Month 6	67	2.28	0.71	0.00	3.00	2.00	94	2.14	0.67	1.00	3.00	2.00
Month 9	63	2.33	0.65	1.00	3.00	2.00	90	2.13	0.66	0.00	3.00	2.00
Month 12	63	2.19	0.72	1.00	3.00	2.00	88	1.97	0.65	1.00	3.00	2.00
Month 15	60	2.20	0.66	1.00	3.00	2.00	85	2.01	0.72	1.00	3.00	2.00
Month 18	60	2.17	0.72	1.00	3.00	2.00	85	2.05	0.71	1.00	3.00	2.00

Use of Sleep Medication

	EMOT						SERV					
Visits	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**
Baseline	84	1.93	1.34	0.00	3.00	3.00	97	1.87	1.34	0.00	3.00	3.00
Cleared	84	2.04	1.31	0.00	3.00	3.00	97	1.92	1.36	0.00	3.00	3.00
Month 3	70	1.81	1.35	0.00	3.00	3.00	95	1.84	1.39	0.00	3.00	3.00
Month 6	67	1.90	1.37	0.00	3.00	3.00	94	1.74	1.41	0.00	3.00	3.00
Month 9	64	1.98	1.23	0.00	3.00	3.00	91	1.74	1.41	0.00	3.00	3.00
Month 12	63	1.90	1.40	0.00	3.00	3.00	88	1.68	1.40	0.00	3.00	2.00
Month 15	61	1.98	1.32	0.00	3.00	3.00	86	1.62	1.37	0.00	3.00	2.00
Month 18	60	1.90	1.36	0.00	3.00	3.00	86	1.62	1.35	0.00	3.00	2.00

Daytime Dysfunction

	EMOT						SERV					
Visits	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**
Baseline	84	1.67	0.80	0.00	3.00	2.00	97	1.49	0.81	0.00	3.00	1.00
Cleared	84	1.86	0.87	0.00	3.00	2.00	97	1.59	0.73	0.00	3.00	1.00
Month 3	70	1.56	0.77	0.00	3.00	1.00	95	1.46	0.68	0.00	3.00	1.00
Month 6	67	1.54	0.82	0.00	3.00	1.00	94	1.46	0.65	0.00	3.00	1.00
Month 9	64	1.66	0.78	0.00	3.00	2.00	91	1.43	0.72	0.00	3.00	1.00
Month 12	63	1.57	0.86	0.00	3.00	1.00	88	1.49	0.74	0.00	3.00	1.00
Month 15	61	1.49	0.79	0.00	3.00	2.00	86	1.38	0.77	0.00	3.00	1.00
Month 18	60	1.38	0.74	0.00	3.00	1.00	86	1.27	0.73	0.00	3.00	1.00

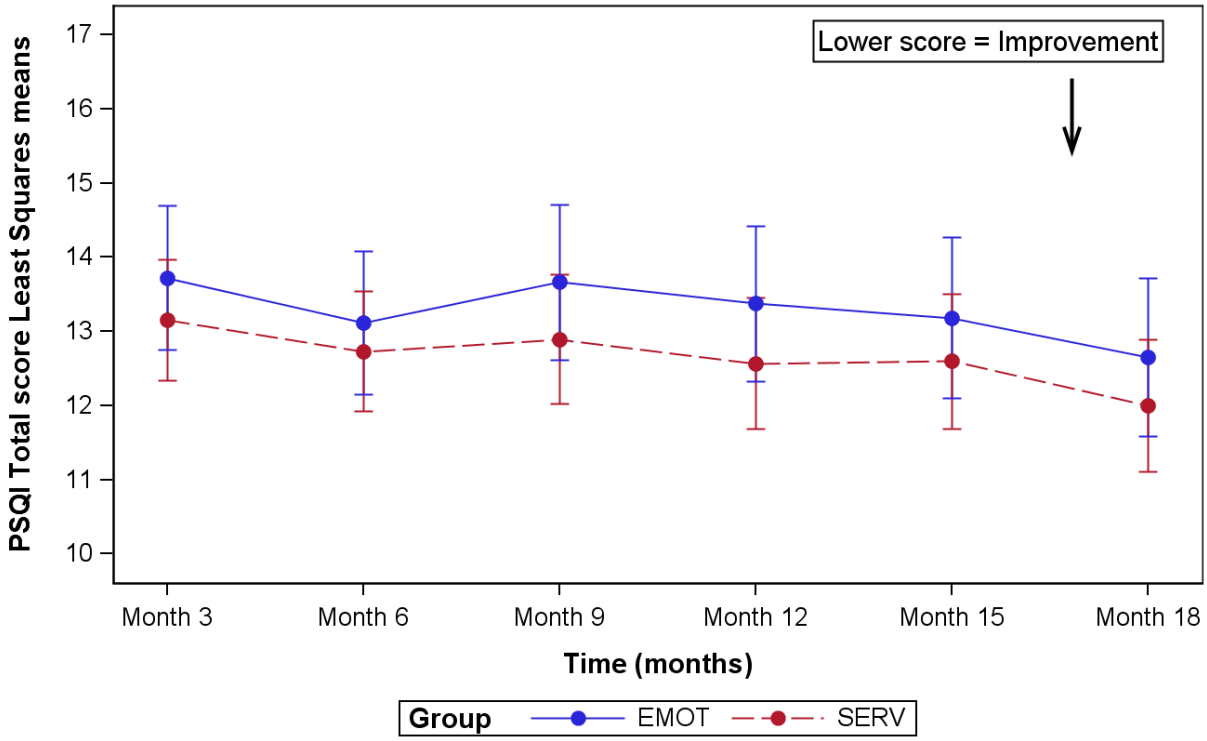
Table XXX. Linear Mixed Repeated Measures model and Random Intercept model results for the PSQI Total score (PPDR)

		Repeated (PPDR)		Random Int (PPDR)	
Outcome	**Effect**	**F statistic**	**P-value**	**F statistic**	**P-value**
PSQI	Baseline score	95.65	<.0001	99.27	<.0001
	Gender	4.19	0.0423	2.26	0.1345
	Center	2.30	0.1040	2.11	0.1246
	Treatment	1.57	0.2113	1.46	0.2291
	Time	3.52	0.0049	3.42	0.0047
	Treatment*Time	0.15	0.9809	0.14	0.9816

Table YYY.1. Effect of SERV Intervention vs. EMOT Intervention for PSQI Total score (PPDR)

			PPDR			
	Outcome Measure	**Population -Model Type**	**Estimate**	**95% CI Lower**	**95% CI Upper**	**P-value**
SERV vs. EMOT over time	PSQI	repeated	-0.6273	-1.6146	0.3600	0.2113
SERV vs. EMOT at 18 months	PSQI	repeated	-0.6514	-1.9361	0.6333	0.3181
SERV vs. EMOT over time	PSQI	random intercept	-0.5988	-1.5784	0.3807	0.2291
SERV vs. EMOT at 18 months	PSQI	random intercept	-0.6197	-1.8559	0.6165	0.3249

Figure YYY.2. PSQI total score Least Squares Means and 95% confidence intervals over time by Treatment from the linear mixed repeated measures model (lower score=improvement; PPDR population)



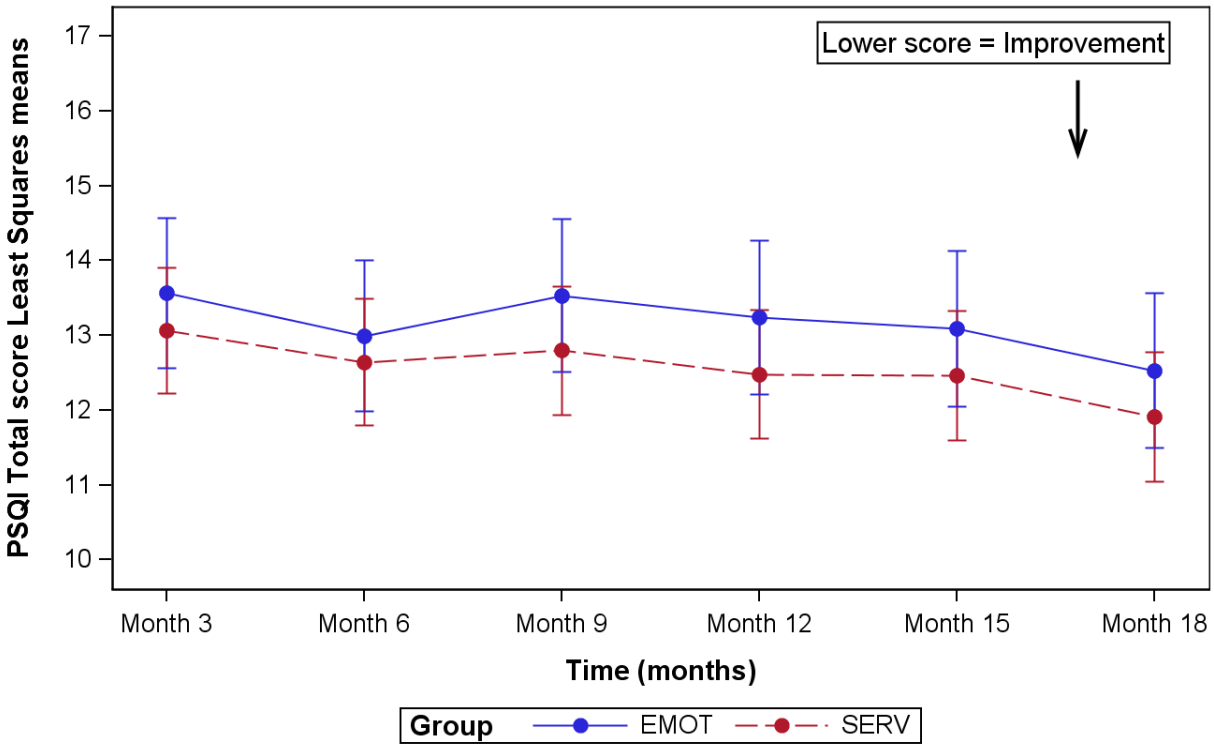
Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

Table YYY.3 PSQI total score Least Squares Means (Adjusted) and 95% confidence intervals over time by Treatment from the linear mixed repeated measures model (lower score=improvement; PPDR population)

	EMOT		SERV	
Time	**N**	**Adjusted Mean (95% CI)**	**N**	**Adjusted Mean (95% CI)**
3	69	13.72 (12.75, 14.69)	95	13.15 (12.34, 13.97)
6	67	13.12 (12.15, 14.08)	94	12.73 (11.92, 13.54)
9	63	13.66 (12.62, 14.70)	90	12.89 (12.02, 13.76)
12	63	13.37 (12.32, 14.42)	88	12.57 (11.69, 13.45)
15	59	13.18 (12.10, 14.27)	85	12.59 (11.69, 13.50)
18	60	12.65 (11.58, 13.72)	85	12.00 (11.10, 12.89)

Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

Figure YYY.4. PSQI total score Least Squares Means and 95% confidence intervals over time by Treatment from the random intercept model (lower score=improvement; PPDR population)



Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

Table YYY.5. PSQI total score Least Squares Means (Adjusted) and 95% confidence intervals over time by Treatment from the random intercept model (lower score=improvement; PPDR population)

	EMOT		SERV	
Time	**N**	**Adjusted Mean (95% CI)**	**N**	**Adjusted Mean (95% CI)**
3	69	13.57 (12.56, 14.57)	95	13.06 (12.22, 13.90)
6	67	12.99 (11.98, 14.00)	94	12.64 (11.79, 13.49)
9	63	13.53 (12.51, 14.55)	90	12.79 (11.94, 13.65)
12	63	13.24 (12.22, 14.26)	88	12.48 (11.62, 13.34)
15	59	13.09 (12.05, 14.13)	85	12.47 (11.60, 13.33)
18	60	12.53 (11.49, 13.56)	85	11.91 (11.04, 12.77)

Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

Table ZZZ. C-SSRS over time by group (PPDR)

Endpoint	Visit	EMOT (n = 84) n (%)	SERV (n = 97) n (%)	Total (n = 181) n (%)
Suicidal Ideation	**Baseline**	13 (15.5)	24 (24.7)	37 (20.4)
	Cleared	22 (26.2)	36 (37.1)	58 (32.0)
	Month 3	21 (30.0)	33 (34.7)	54 (32.7)
	Month 6	18 (26.9)	21 (22.3)	39 (24.2)
	Month 9	18 (28.1)	21 (23.1)	39 (25.2)
	Month 12	18 (28.6)	23 (26.1)	41 (27.2)
	Month 15	19 (31.1)	19 (22.1)	38 (25.9)
	Month 18	17 (28.3)	11 (12.9)	28 (19.3)
Suicidal Behavior	**Baseline**	0 (0.0)	0 (0.0)	0 (0.0)
	Cleared	1 (1.2)	1 (1.0)	2 (1.1)
	Month 3	1 (1.4)	1 (1.1)	2 (1.2)
	Month 6	2 (3.0)	2 (2.1)	4 (2.5)
	Month 9	1 (1.6)	1 (1.1)	2 (1.3)
	Month 12	1 (1.6)	0 (0.0)	1 (0.7)
	Month 15	2 (3.3)	0 (0.0)	2 (1.4)
	Month 18	0 (0.0)	0 (0.0)	0 (0.0)
Suicidal Ideation or Behavior (SBI)	**Baseline**	13 (15.5)	24 (24.7)	37 (20.4)
	Cleared	22 (26.2)	36 (37.1)	58 (32.0)
	Month 3	21 (30.0)	33 (34.7)	54 (32.7)
	Month 6	18 (26.9)	21 (22.3)	39 (24.2)
	Month 9	18 (28.1)	21 (23.1)	39 (25.2)
	Month 12	18 (28.6)	23 (26.1)	41 (27.2)
	Month 15	19 (31.1)	19 (22.1)	38 (25.9)
	Month 18	17 (28.3)	11 (12.9)	28 (19.3)

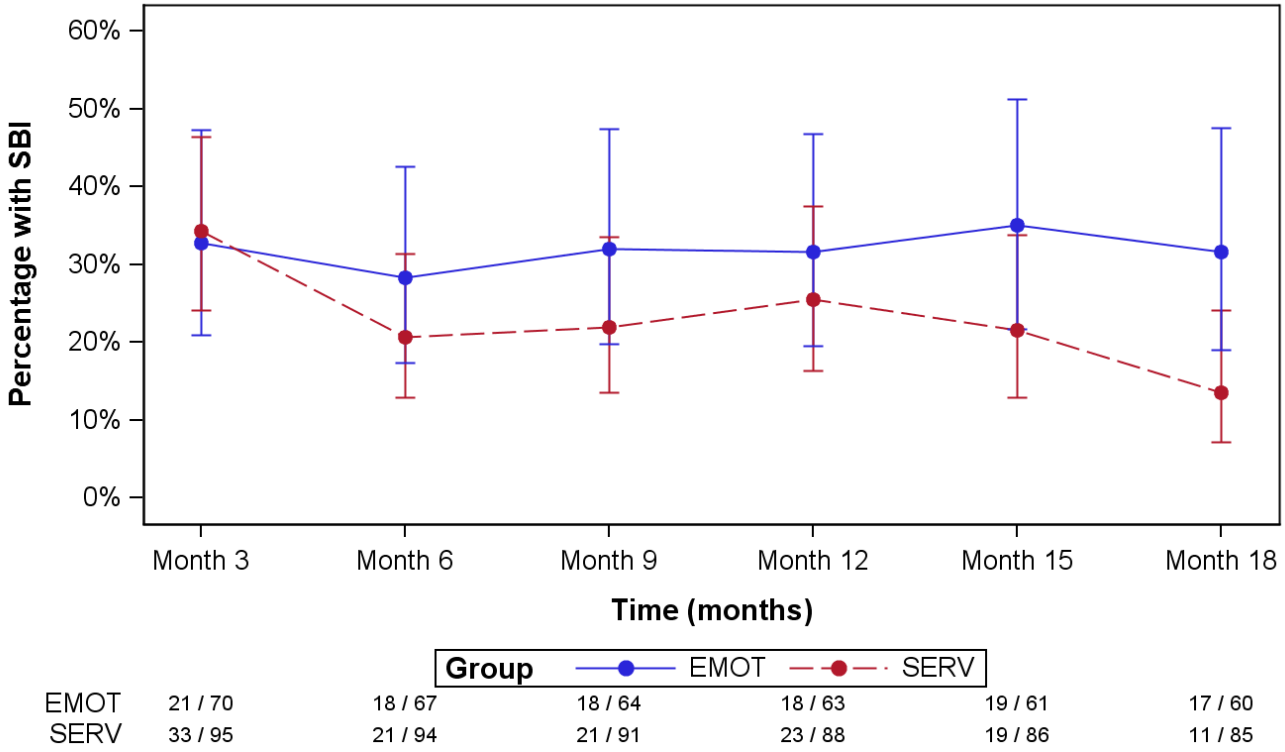
Table AAAA. Generalized Linear Mixed Repeated Measures model results for C-SSRS SBI (PPDR)

		Repeated (PPDR)	
Outcome	**Effect**	**F statistic**	**P-value**
C-SSRS SBI	Baseline score	13.98	0.0003
	Gender	2.26	0.1349
	Center	1.21	0.3012
	Treatment	2.07	0.1523
	Time	2.31	0.0469
	Treatment*Time	1.78	0.1208

Table BBBB.1. Effect of SERV Intervention vs. EMOT Intervention for C-SSRS SBI (PPDR)

	Outcome Measure	Population-Model Type	PPDR			
			Estimate	95% CI Lower	95% CI Upper	P-value
SERV vs. EMOT over time	C-SSRS SBI	repeated	-0.4858	-1.1528	0.1812	0.1523
SERV vs. EMOT at 18 months	C-SSRS SBI	repeated	-1.0812	-2.0052	-0.1573	0.0221

Figure BBBB.2. C-SSRS Suicidal Behavior or Ideation (SBI) rate Least Squares Means (proportions) and 95% confidence intervals over time by Treatment from the linear mixed repeated measures model (PPDR population)



Note: Participants at risk for each time point: n / N where n=number of participants with SBI in the category, and N=total number of participants in the category. Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

Table BBBB.3. C-SSRS Suicidal Behavior or Ideation (SBI) rate Least Squares Means (Adjusted, proportions) and 95% confidence intervals over time by Treatment from the linear mixed repeated measures model (PPDR population)

	EMOT		SERV	
Time	**n / N**	**Adjusted Proportions (95% CI)**	**n / N**	**Adjusted Proportions (95% CI)**
Month 3	21 / 70	32.74 (20.88, 47.31)	33 / 95	34.34 (24.04, 46.35)
Month 6	18 / 67	28.30 (17.37, 42.57)	21 / 94	20.69 (12.96, 31.38)
Month 9	18 / 64	32.02 (19.79, 47.36)	21 / 91	21.93 (13.54, 33.50)
Month 12	18 / 63	31.56 (19.51, 46.72)	23 / 88	25.49 (16.38, 37.40)
Month 15	19 / 61	35.05 (21.70, 51.24)	19 / 86	21.54 (12.90, 33.73)
Month 18	17 / 60	31.58 (19.04, 47.53)	11 / 85	13.54 (7.18, 24.08)

Note: Participants at risk for each time point: n / N where n=number of participants with SBI in the category, and N=total number of participants in the category. Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

Table CCCC. Unadjusted PCL-5 (lower score = better) over time by group (PPDR)

	EMOT						SERV					
Visits	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**
Baseline	84	46.98	14.70	7.00	80.00	48.50	97	48.33	15.66	12.00	77.00	50.00
Cleared	84	49.57	14.16	13.00	78.00	50.00	97	49.85	15.14	9.00	75.00	50.00
Month 3	70	41.89	15.89	8.00	74.00	45.00	95	41.54	15.14	7.00	76.00	40.00
Month 6	67	39.10	16.81	3.00	79.00	38.00	94	39.39	14.87	10.00	79.00	37.00
Month 9	64	41.11	15.76	7.00	74.00	41.00	91	38.23	15.11	7.00	73.00	37.00
Month 12	63	39.75	17.96	2.00	79.00	42.00	88	35.39	15.49	9.00	73.00	31.50
Month 15	61	40.64	16.82	1.00	72.00	43.00	86	35.86	16.29	10.00	75.00	33.50
Month 18	60	34.72	17.00	2.00	65.00	33.50	85	31.28	14.71	9.00	72.00	28.00

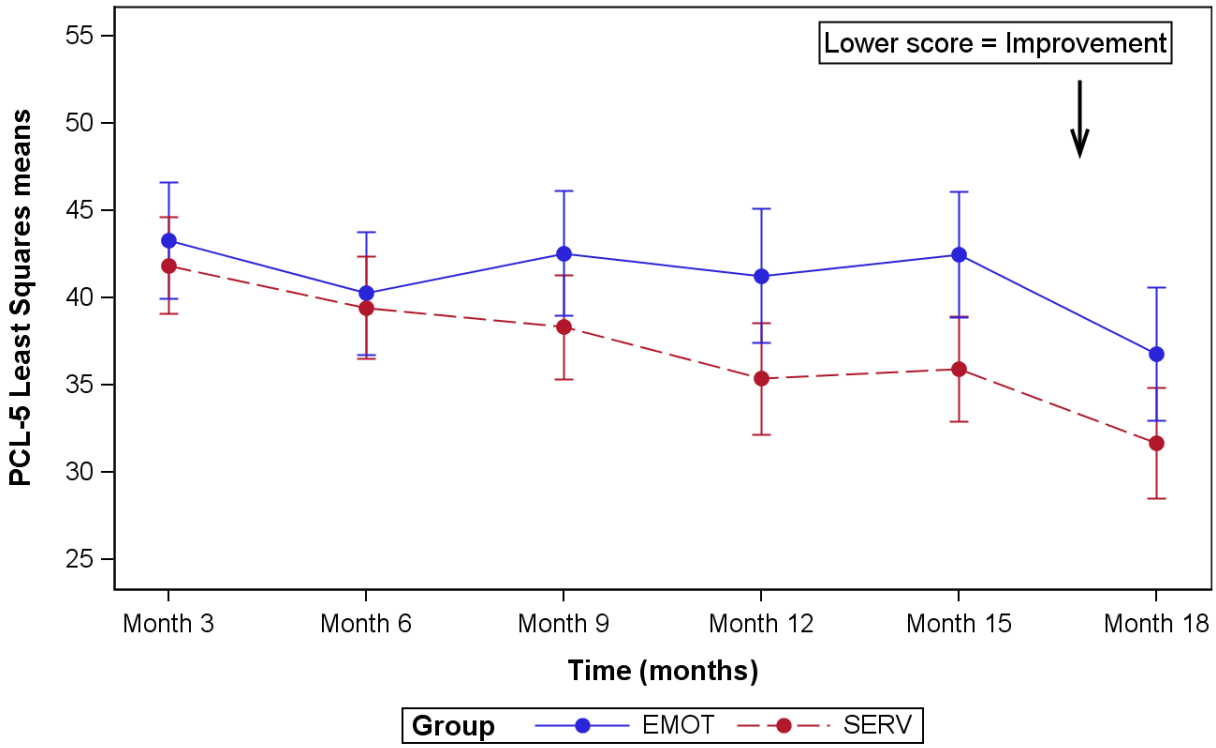
Table DDDD. Linear Mixed Repeated Measures model and Random Intercept model results for the PCL-5 (PPDR)

		Repeated (PPDR)		Random Int (PPDR)	
Outcome	**Effect**	**F statistic**	**P-value**	**F statistic**	**P-value**
PCL-5	Baseline score	109.92	<.0001	101.72	<.0001
	Gender	1.40	0.2381	0.78	0.3787
	Center	3.20	0.0433	3.41	0.0353
	Treatment	4.96	0.0273	4.81	0.0298
	Time	14.39	<.0001	17.33	<.0001
	Treatment*Time	2.36	0.0431	3.11	0.0087

Table EEEE.1. Effect of SERV Intervention vs. EMOT Intervention for PCL-5 (PPDR)

	Outcome Measure	Population-Model Type	PPDR			
			Estimate	95% CI Lower	95% CI Upper	P-value
SERV vs. EMOT over time	PCL-5	repeated	-4.0123	-7.5701	-0.4545	0.0273
SERV vs. EMOT at 18 months	PCL-5	Repeated	-5.1123	-9.7130	-0.5115	0.0297
SERV vs. EMOT over time	PCL-5	random intercept	-3.9218	-7.4546	-0.3890	0.0298
SERV vs. EMOT at 18 months	PCL-5	random intercept	-4.9672	-9.2869	-0.6474	0.0243

Figure EEEE.2 PCL-5 score Least Squares Means and 95% confidence intervals over time by Treatment from the linear mixed repeated measures model (lower score=improvement; PPDR population)



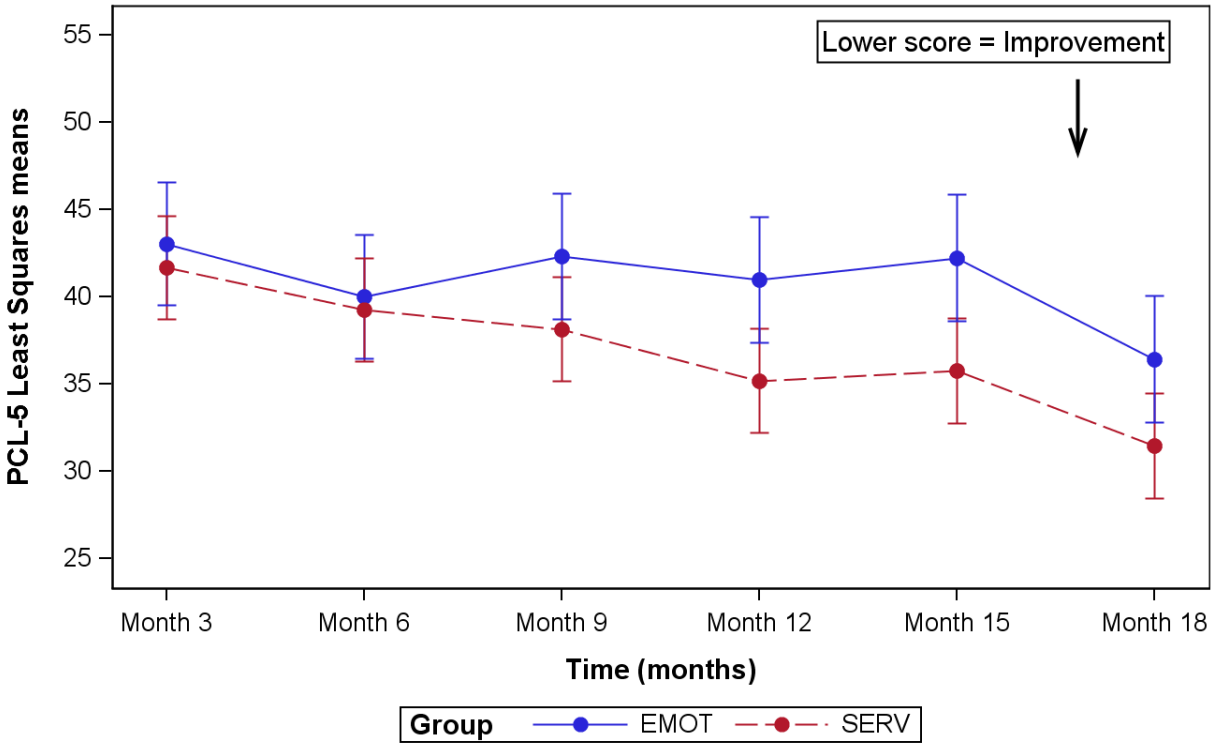
Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

Table EEEE.3. PCL-5 score Least Squares Means (Adjusted) and 95% confidence intervals over time by Treatment from the linear mixed repeated measures model (lower score=improvement; PPDR population)

	EMOT		SERV	
Time	**N**	**Adjusted Mean (95% CI)**	**N**	**Adjusted Mean (95% CI)**
3	70	43.30 (39.98, 46.62)	95	41.85 (39.08, 44.62)
6	67	40.27 (36.76, 43.77)	94	39.43 (36.51, 42.35)
9	64	42.54 (38.98, 46.11)	91	38.32 (35.35, 41.28)
12	63	41.25 (37.41, 45.09)	88	35.37 (32.16, 38.57)
15	61	42.48 (38.89, 46.08)	86	35.92 (32.94, 38.91)
18	60	36.79 (32.97, 40.62)	85	31.68 (28.50, 34.87)

Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

Figure EEEE.4. PCL-5 score Least Squares Means and 95% confidence intervals over time by Treatment from the random intercept model (lower score=improvement; PDR population)



Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

Table EEEE.5. PCL-5 score Least Squares Means (Adjusted) and 95% confidence intervals over time by Treatment from the random intercept model (lower score=improvement; PPDR population)

	EMOT		SERV	
Time	N	Adjusted Mean (95% CI)	N	Adjusted Mean (95% CI)
3	70	43.04 (39.52, 46.56)	95	41.68 (38.73, 44.62)
6	67	40.02 (36.47, 43.57)	94	39.26 (36.30, 42.22)
9	64	42.33 (38.75, 45.91)	91	38.15 (35.18, 41.13)
12	63	40.97 (37.37, 44.56)	88	35.19 (32.20, 38.19)
15	61	42.24 (38.62, 45.85)	86	35.75 (32.74, 38.76)
18	60	36.43 (32.80, 40.05)	85	31.46 (28.45, 34.47)

Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

Table FFFF. CAPS PTSD status* (PPDR)

	EMOT		SERV		Total		
	Present	Absent	Present	Absent	Present	Absent	
Visit	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	P-value
Month 15	45 (73.8)	16 (26.2)	58 (68.2)	27 (31.8)	103 (70.5)	43 (29.5)	0.4693

*Presence of PTSD was defined as CAPS criteria A-G being satisfied.

Table GGGG. Unadjusted CAPS total symptom (lower score = better) severity score (PPDR)

	EMOT						SERV					
Visit	N	Mean	SD	Min	Max	Median	N	Mean	SD	Min	Max	Median
Screening	84	40.08	10.32	17	64	39	97	39.59	9.38	20	63	40
Month 15	61	34.46	13.69	6	66	35	85	31.68	11.94	7	65	33

Table HHHH. Unadjusted PHQ-9 (lower score = better) over time by group (PPDR)

	EMOT						SERV					
Visits	n	Mean	SD	Min	Max	Median	n	Mean	SD	Min	Max	Median
Baseline	84	13.08	5.94	0.00	25.00	13.00	97	12.79	5.85	0.00	25.00	12.00
Cleared	84	13.57	6.14	0.00	25.00	14.00	97	13.35	5.44	2.00	26.00	13.00
Month 3	70	11.33	6.14	0.00	27.00	11.00	95	10.95	5.47	0.00	24.00	11.00
Month 6	67	10.45	6.09	0.00	26.00	9.00	94	10.03	5.07	0.00	23.00	9.00
Month 9	64	11.42	6.09	0.00	25.00	11.00	91	9.49	4.82	0.00	23.00	9.00
Month 12	63	11.06	6.45	0.00	23.00	10.00	88	9.90	5.68	0.00	22.00	9.00
Month 15	61	11.23	6.19	0.00	24.00	10.00	85	9.61	5.66	0.00	24.00	9.00
Month 18	60	9.10	6.14	0.00	25.00	8.50	85	8.09	4.46	0.00	21.00	8.00

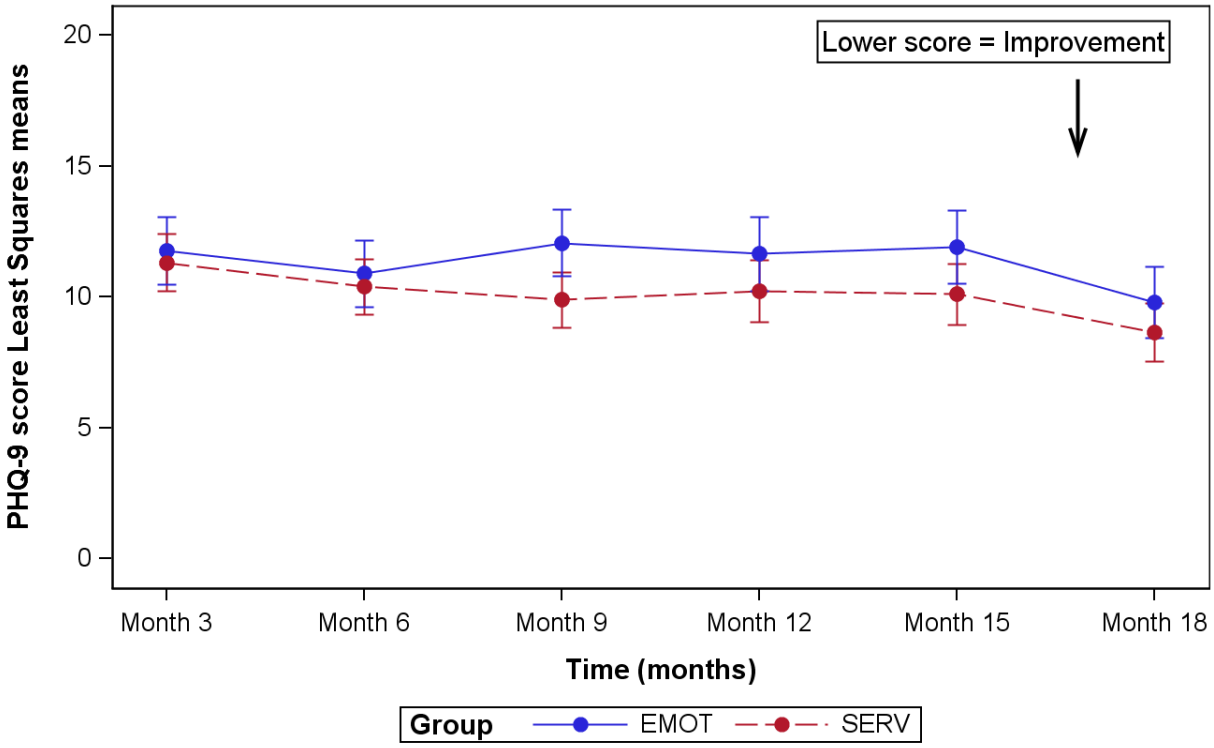
Table IIII. Linear Mixed Repeated Measures model and Random Intercept model results for the PHQ-9 (PPDR)

		Repeated (PPDR)		Random Int (PPDR)	
Outcome	**Effect**	**F statistic**	**P-value**	**F statistic**	**P-value**
PHQ-9	Baseline score	69.23	<.0001	70.65	<.0001
	Gender	3.84	0.0518	3.47	0.0642
	Center	4.69	0.0106	4.86	0.0089
	Treatment	3.70	0.0564	3.70	0.0562
	Time	8.68	<.0001	9.12	<.0001
	Treatment*Time	1.69	0.1402	1.77	0.1168

Table JJJJ.1. Effect of SERV Intervention vs. EMOT Intervention for PHQ-9 (PPDR)

	Outcome Measure	Population-Model Type	PPDR			
			Estimate	**95% CI Lower**	**95% CI Upper**	**P-value**
SERV vs. EMOT over time	PHQ-9	repeated	-1.2509	-2.5361	0.03437	0.0564
SERV vs. EMOT at 18 months	PHQ-9	repeated	-1.1561	-2.7770	0.4648	0.1608
SERV vs. EMOT over time	PHQ-9	random intercept	-1.2461	-2.5253	0.03315	0.0562
SERV vs. EMOT at 18 months	PHQ-9	random intercept	-1.1589	-2.7580	0.4403	0.1550

Figure JJJJ.2. PHQ-9 score Least Squares Means and 95% confidence intervals over time by Treatment from the linear mixed repeated measures model (lower score=improvement; PPDR population)



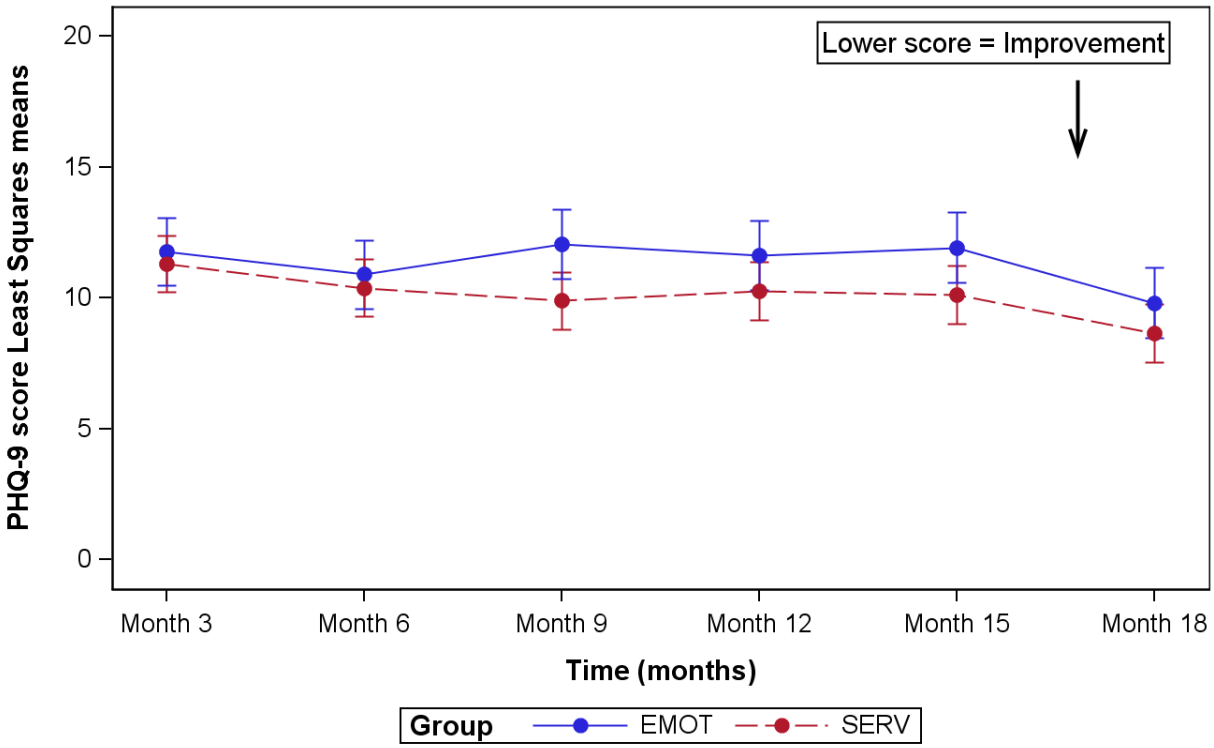
Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

Table JJJJ.3. PHQ-9 score Least Squares Means (Adjusted) and 95% confidence intervals over time by Treatment from the linear mixed repeated measures model (lower score=improvement; PPDR population)

	EMOT		SERV	
Time	**N**	**Adjusted Mean (95% CI)**	**N**	**Adjusted Mean (95% CI)**
3	70	11.76 (10.47, 13.05)	95	11.31 (10.23, 12.39)
6	67	10.89 (9.62, 12.16)	94	10.38 (9.32, 11.44)
9	64	12.05 (10.79, 13.32)	91	9.89 (8.84, 10.95)
12	63	11.64 (10.24, 13.05)	88	10.22 (9.04, 11.39)
15	61	11.91 (10.53, 13.29)	85	10.10 (8.94, 11.25)
18	60	9.80 (8.45, 11.15)	85	8.64 (7.52, 9.77)

Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

Figure JJJJ.4. PHQ-9 score Least Squares Means and 95% confidence intervals over time by Treatment from the random intercept model (lower score=improvement; PPDR population)



Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

Table JJJJ.5. PHQ-9 score Least Squares Means (Adjusted) and 95% confidence intervals over time by Treatment from the random intercept model (lower score=improvement; PPDR population)

	EMOT		SERV	
Time	**N**	**Adjusted Mean (95% CI)**	**N**	**Adjusted Mean (95% CI)**
3	70	11.76 (10.47, 13.05)	95	11.30 (10.21, 12.38)
6	67	10.89 (9.59, 12.20)	94	10.37 (9.28, 11.46)
9	64	12.04 (10.72, 13.36)	91	9.88 (8.79, 10.98)
12	63	11.63 (10.31, 12.96)	88	10.25 (9.15, 11.36)
15	61	11.92 (10.59, 13.26)	85	10.12 (9.01, 11.23)
18	60	9.80 (8.46, 11.14)	85	8.64 (7.53, 9.75)

Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

Table KKKK. DAR scores (lower score = better) over time by group (PPDR)

	EMOT						SERV					
Visits	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**	**n**	**Mean**	**SD**	**Min**	**Max**	**Median**
Baseline	84	23.82	14.64	0.00	54.00	22.50	97	21.85	15.07	0.00	56.00	20.00
Cleared	84	24.99	15.27	0.00	54.00	22.50	97	23.89	15.21	0.00	52.00	25.00
Month 3	70	23.99	16.03	0.00	54.00	21.50	95	22.14	14.28	0.00	52.00	22.00
Month 6	67	21.90	16.56	0.00	56.00	17.00	94	20.35	13.75	0.00	56.00	17.00
Month 9	64	24.28	15.97	0.00	56.00	23.50	91	19.47	13.28	0.00	53.00	18.00
Month 12	63	23.62	15.53	0.00	56.00	24.00	88	18.33	14.78	0.00	56.00	15.00
Month 15	61	22.46	17.08	0.00	53.00	19.00	86	17.42	14.36	0.00	56.00	14.50
Month 18	60	19.90	16.52	0.00	55.00	16.00	85	15.51	14.21	0.00	56.00	11.00

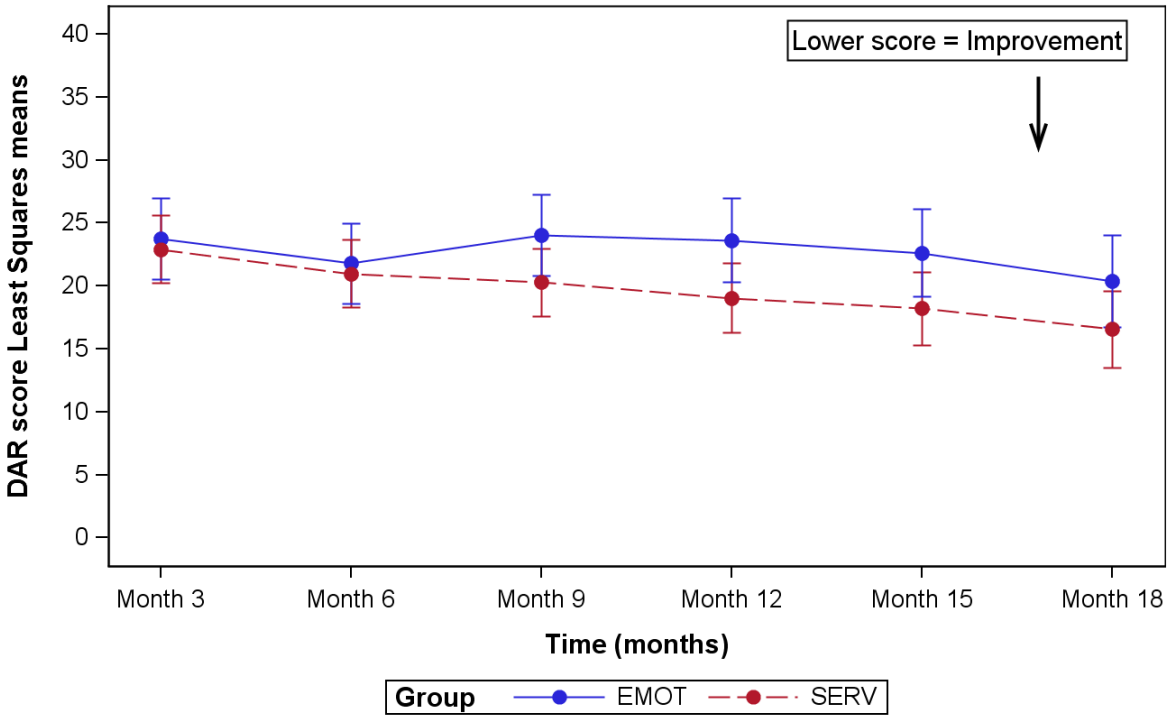
Table LLLL. Linear Mixed Repeated Measures model and Random Intercept model results for the DAR (PPDR)

		Repeated (PPDR)		Random Int (PPDR)	
Outcome	**Effect**	**F statistic**	**P-value**	**F statistic**	**P-value**
DAR	Baseline score	97.50	<.0001	91.34	<.0001
	Gender	0.92	0.3390	0.52	0.4709
	Center	7.05	0.0012	8.30	0.0004
	Treatment	3.09	0.0805	3.02	0.0839
	Time	5.59	<.0001	8.35	<.0001
	Treatment*Time	1.61	0.1606	2.41	0.0353

Table MMMM.1. Effect of SERV Intervention vs. EMOT intervention for DAR (PPDR)

	Outcome Measure	Population-Model Type	PPDR			
			Estimate	**95% CI Lower**	**95% CI Upper**	**P-value**
SERV vs. EMOT over time	DAR	repeated	-3.0327	-6.4376	0.3723	0.0805
SERV vs. EMOT at 18 months	DAR	repeated	-3.8260	-8.2092	0.5572	0.0866
SERV vs. EMOT over time	DAR	random intercept	-2.9727	-6.3483	0.4028	0.0839
SERV vs. EMOT at 18 months	DAR	random intercept	-3.7469	-7.7230	0.2292	0.0647

Figure MMMM.2. DAR score Least Squares Means and 95% confidence intervals over time by Treatment from the linear mixed repeated measures model (lower score=improvement; PPDR population)



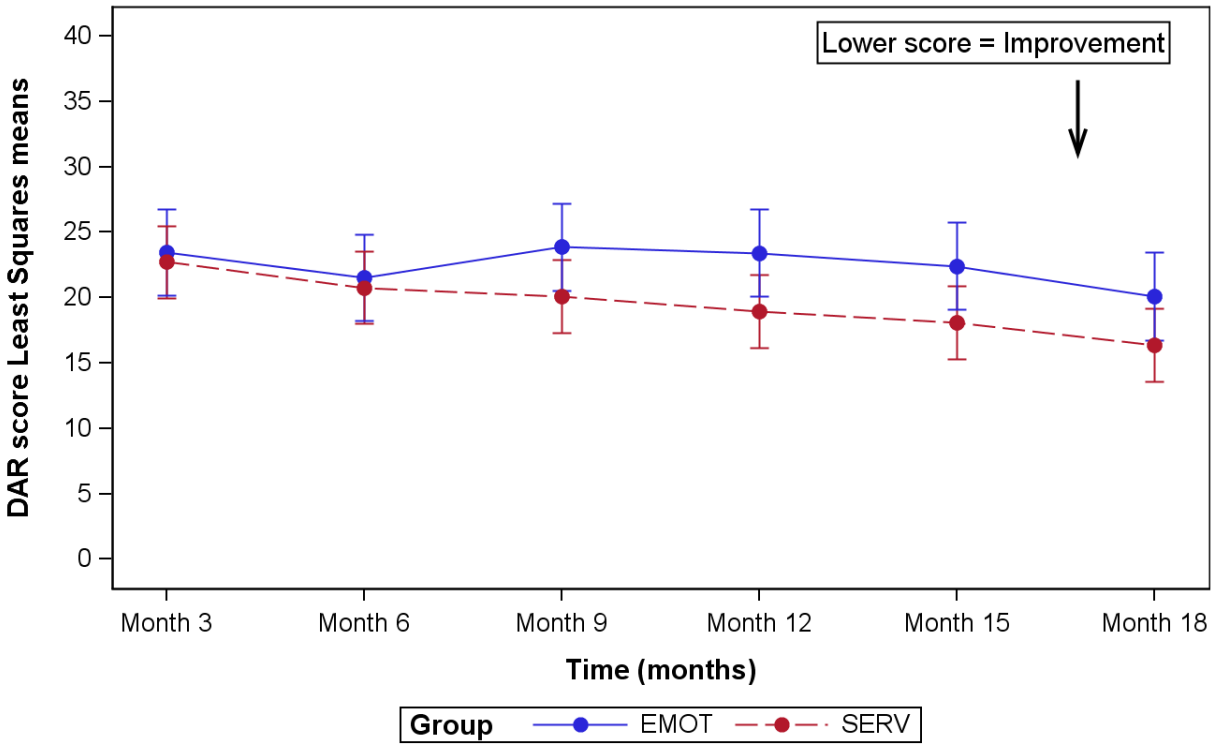
Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

Table MMMM.3. DAR score Least Squares Means (Adjusted) and 95% confidence intervals over time by Treatment from the linear mixed repeated measures model (lower score=improvement; PPDR population)

	EMOT		SERV	
Time	**N**	**Adjusted Mean (95% CI)**	**N**	**Adjusted Mean (95% CI)**
3	70	23.71 (20.49, 26.93)	95	22.91 (20.21, 25.61)
6	67	21.77 (18.58, 24.96)	94	20.96 (18.30, 23.63)
9	64	24.04 (20.81, 27.27)	91	20.27 (17.58, 22.96)
12	63	23.61 (20.28, 26.94)	88	19.04 (16.26, 21.82)
15	61	22.62 (19.14, 26.10)	86	18.20 (15.29, 21.11)
18	60	20.39 (16.74, 24.03)	85	16.56 (13.52, 19.61)

Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

Figure MMMM.4. DAR score Least Squares Means and 95% confidence intervals over time by Treatment from the random intercept model (lower score=improvement; PPDR population)



Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

Table MMMM.5. DAR score Least Squares Means (Adjusted) and 95% confidence intervals over time by Treatment from the random intercept model (lower score=improvement; PPDR population)

	EMOT		SERV	
Time	**N**	**Adjusted Mean (95% CI)**	**N**	**Adjusted Mean (95% CI)**
3	70	23.46 (20.19, 26.73)	95	22.71 (19.96, 25.45)
6	67	21.52 (18.22, 24.82)	94	20.76 (18.00, 23.52)
9	64	23.85 (20.53, 27.18)	91	20.08 (17.31, 22.86)
12	63	23.39 (20.05, 26.72)	88	18.92 (16.13, 21.71)
15	61	22.40 (19.05, 25.74)	86	18.05 (15.26, 20.85)
18	60	20.11 (16.75, 23.46)	85	16.36 (13.56, 19.16)

Note: Model least squares means were adjusted for baseline score, gender, center, time, treatment group, and the time by treatment group interaction. As these post-pairing means were adjusted for the baseline score, the baseline time point is not presented. However, baseline and clearing data ("Cleared") are presented in tables of unadjusted descriptive statistics at each visit. Visits occurred at 3-month intervals after dog pairing.

Part B – Attrition and Missing Data Analyses

Table NNNN. Adjusted Odds Ratios and 95% Confidence Intervals from a multivariate logistic regression model of attrition status (probability modeled was participants not completing the study)(PP)

Effect	Odds Ratio	95% Confidence Limits	
		Lower	Upper
Baseline WHO-DAS 2.0 score	1.019	0.978	1.062
Baseline PCL-5 score	0.973	0.935	1.012
Age	0.999	0.965	1.034
Center 508 (vs 648)	1.901	0.600	6.028
Center 584 (vs 648)	0.764	0.216	2.702
Female	0.493	0.131	1.857
Married	1.125	0.443	2.857
SERV vs. EMOT	0.599	0.072	4.972
SERV * Baseline WHO-DAS score interaction	0.990	0.939	1.044

Table OOOO. Treatment effect based on available data and imputed data (PPDR)

	Available data				Imputed Data			
Outcome	Estimate	Lower 95% CI	Upper 95% CI	P-value	Estimate	Lower 95% CI	Upper 95% CI	P-value
WHO-DAS 2.0	-4.5669	-9.7765	0.6427	0.0853	-4.1886	-9.6864	1.3092	0.1343
PCS	-1.1434	-4.1105	1.8237	0.4477	-1.0930	-4.5065	2.3205	0.5254
MCS	1.7179	-1.4900	4.9257	0.2917	0.9544	-2.8735	4.7823	0.6191
PSQI	-0.6514	-1.9361	0.6333	0.3181	-0.5480	-1.8024	0.7065	0.3907
PHQ-9	-1.1561	-2.7770	0.4648	0.1608	-1.3173	-3.0033	0.3687	0.1246
PCL-5	-5.1123	-9.7130	-0.5115	0.0297	-4.8314	-9.6870	0.0242	0.0511
C-SSRS	-1.0812	-2.0052	-0.1573	0.0221	-0.9238	-1.7830	-0.0646	0.0351
DAR	-3.8260	-8.2092	0.5572	0.0866	-3.4160	-7.4221	0.5900	0.0946

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