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The Psychological Impact of Testosterone Replacement Therapy in Middle-Aged Men

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Abstract

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Dissertation Submitted in Partial Fulfillment

of the Requirements for the Degree of

Doctor of Philosophy

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Abstract

Decreased testosterone levels (hypogonadism) in middle-aged men (aged 45–64) has been associated with increased levels of depression. Studies have suggested that increases in anxiety and/or attention problems may also be associated with hypogonadism but have not provided empirical evidence to support these suggestions. The purpose of this quantitative study was to examine depression, anxiety, and attention problems in middle-aged men using a psychological self-report inventory. The theoretical model used in this study was the biomedical model, which combined pharmacological treatment with psychological self-report inventories to determine if there was an association or relationship between the testosterone levels in men and the psychological distress experienced by men who have become hypogonadal. A total of 179 males were recruited through local physicians. There was a statistically significant difference and a small size effect in the level of depression, anxiety, and/or attention issues experienced by those who were receiving TRT versus those who were not. This study may provide some guidance to medical clinicians, such as psychiatrists, primary-care physicians, and endocrinologists, as well as clinical psychologists who see middle-aged men in their practice settings.

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Dedication

When I began this journey to become a clinical psychologist, I did it for my two sons in hopes that they would be inspired to pursue higher education, as well as academic and professional excellence in their lives. This dissertation is dedicated to Vance R. Coles and Gregory E. Coles Jr. These young men mean more to me than life itself.

Acknowledgments

I would like to thank Dr. Michael Plasay (Chair) and Dr. Mitchell Hicks (Second Committee Member) for their efforts, work, and support in assisting me in completing this dissertation, and for pushing me in the process of becoming the very best scholar-practitioner possible. I want to express my gratitude to Dr. Rodney Ford who was my University Research Reviewer (URR) for his support in this process as well. Also, I wish to thank Dr. Robert Kaplan, Dr. Karen Broer, and Dr. Patrick White who were my clinical supervisors. They were instrumental in granting me the opportunity to complete all of the fieldwork requirements necessary for completion of this degree. These clinicians not only taught me how to be an excellent clinician, but also challenged me to stretch and grow through the clinical teaching-learning process. Finally, I wish to thank Dr. Christine Collis, my best friend, who was and continues to be a huge source of moral support and encouragement to persevere through this most challenging academic degree pursuit, as well as in life generally.

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Chapter 1: Introduction to the Study

There is still some debate among medical scholars as to whether testosterone replacement therapy (TRT) can have a positive impact on depression and other mental health issues faced by men in midlife and beyond (Charlton, 2004; Rizvi et al., 2010). However, there is a growing body of medical research studies that suggest that TRT can reduce some of the mental health issues middle-aged (i.e., ages 45-64) and older men (i.e., ages 65 and older) experience as they move through the life span (Charlton, 2004; Rizvi et al., 2010). The focus of this study was men in middle age and the impact of TRT on depression, anxiety, and attention problems among them. If TRT can have a mitigating effect on depression, anxiety, and/or attention problems in middle-aged men, there are clinical implications for how clinical psychologists conduct initial evaluations and data gathering, as well as how treatment plans are developed for these men. This has the potential to positively impact such men in the United States and in other developed nations around the world.

The sections in this chapter include Background, Problem Statement, Purpose of the Study, Research Questions and Hypotheses, Theoretical and Conceptual Framework, Nature of the Study, Definition of Terms, Assumptions, Scope and Delimitations, Limitations, Significance, and Summary.

Background

There is an incremental decline in the testicular function of men between the ages of 25 and 75, and this decline tends to peak between the ages of 45 and 50 (Charlton, 2004). The concentration of serum bioavailable testosterone (BT) can decrease as much

as 50% during the years of incremental decline, although there can be significant variation between individual men (Charlton, 2004). It should be noted that the incremental decline of testosterone in men over decades is very different from the hormonal decline women experience during menopause, and the two should not be likened to one another (Charlton, 2004; Newhart, 2013). Terms such as *male menopause*, *andropause*, and the like are misnomers, as these terms erroneously suggest that what men experience in middle age is synonymous to menopause experienced by women in middle age (Charlton, 2004; Newhart, 2013). The consequence of not identifying hypogonadism in middle-aged men has resulted in the erroneous assumption that changes in the state of mind or mood in middle age is simply the result of the aging process, and therefore, not treatable (Charlton, 2004). Sadly, many middle-aged men who have hypogonadism may suffer in silence, believing that there is no hope of improving their state of mind and resulting quality of life they experience (Charlton, 2004).

Very little research had been done on middle-aged men with respect to the impact of TRT on mental health issues beyond depression (Moffat et al., 2002; Rizvi et al., 2010; Wang et al., 2000; Wu et al., 2010) at the time the literature review for this study was conducted. Also, the existing literature tended to focus on testosterone threshold levels at which men may begin experiencing mental health concerns that tend to arise as men move through the life span (P. B. Gray et al., 2005; Hintikka et al., 2009; Moffat et al, 2002; Rizvi et al., 2010; Wang, Catlin, Demers, Starcevic, & Swerdloff, 2004; Wang et al., 2000; Wu et al., 2010). This study focused on depression, anxiety, and attention issues experienced by men in middle age who were receiving maintenance levels of TRT

versus those who were not. In contemporaneously existing literature, no study such this study was found. The goal of the clinical psychologist is to help his/her patient feel less of the negative distress resulting from mental-health issues such as depression, anxiety, or attention problems (MacLeod & Moore, 2000). This study is needed so that psychologists and medical clinicians alike might have another tool to enhance the psychological state of mind experienced by their middle-aged male patients who may experience issues with depression, anxiety, and/or attention.

Problem Statement

The problem that was addressed by this study was that as men move through the life span, many begin to experience or have an increased experience of mental-health issues such as depression, anxiety, and attention problems (Charlton, 2004). The majority of research studies, as they pertain to hypogonadism, or low testosterone, were conducted by medical research scholars (P. B. Gray et al., 2005; Hintikka et al., 2009; Moffat et al, 2002; Rizvi et al., 2010; Wang et al., 2004; Wang et al., 2000; Wu et al., 2010). Much of this scholarly literature was focused on determining specific testosterone thresholds at which men may experience such psychological symptoms as depression, loss of energy/fatigue, irritability, or diminished cognitive function (P. B. Gray et al., 2005; Hintikka et al., 2009; Moffat et al, 2002; Rizvi et al., 2010; Wang et al., 2004; Wang et al., 2000; Wu et al., 2010). Notwithstanding the fact that there was very little medical research about the psychological symptoms middle-aged men may experience as they move through the life span related to a decrease in testosterone levels, scholars in clinical psychology have done very little, if any, research on the psychological impact of TRT in

middle-aged men who experience depression, anxiety, and/or attention problems (P. B. Gray et al., 2005; Hintikka et al., 2009; Moffat et al, 2002; Rizvi et al., 2010; Wang et al., 2004; Wang et al., 2000; Wu et al., 2010). As is presented in Chapter 2, there is still some debate among medical researchers as to whether treatment with TRT can have a beneficial impact relative to the psychological state of mind of men diagnosed with hypogonadism (Wu et al., 2010).

The larger question for clinical psychologists, rather than whether or not there is an association between testosterone levels in a man's body and his mood, is whether middle-aged men who are receiving maintenance level TRT versus men who are not receiving TRT experience a different state of mind in relation to depression, anxiety, and/or attention problems (P. B. Gray et al., 2005; Hintikka et al., 2009; Moffat et al, 2002; Rizvi et al., 2010; Wang et al., 2004; Wang et al., 2000; Wu et al., 2010). The question of concern to clinical psychologists, and other clinicians who treat middle-aged men is, “Does TRT reduce symptoms of depression, anxiety, and/or attention problems experienced by middle-aged men?”

Purpose of the Study

The purpose of this quantitative study was to discover any clinically significant differences in depression, anxiety, and/or attention problems experienced by middle-aged men who receive maintenance level doses of TRT versus middle-aged men who do not receive maintenance level doses of TRT. More specifically, as men move through the life span many complain of increased depression, anxiety, and attention problems, especially beginning in middle age (Charlton, 2004). The administration of testosterone, known as

BT or free testosterone (FT), appears to reduce negative aspects of psychological state of mind while increasing some of the positive aspects, which has been shown in clinical trials involving middle-aged men as the sample population (Hijazi & Cunningham, 2005). Cognitive function decreases as men move along their life span (Hijazi & Cunningham, 2005). Vascular and/or degenerative diseases cause anatomic and nervous-system changes, which when combined with age-related decreases in BT cause functional changes in cognition (Hijazi, & Cunningham, 2005).

If middle-aged men can be identified who are experiencing increased depression, anxiety, and/or attention problems, which may be symptomatic of hypogonadism, then they can potentially be treated and have a clinically significant improvement in their state of mind.

Research Question and Hypotheses

The research question addressed in this study was: Do middle-aged men who receive maintenance levels of TRT (i.e., TRT for no less than 1 year) experience a difference in levels depression, anxiety, or attention problems than do middle-aged men who do not receive TRT?

$H_0$1*:* There was no difference in the level of depression, experienced by middle-aged men who are receiving maintenance levels of TRT versus men who are not receiving TRT.

$H_1$1: There was a difference in the level of depression experienced by middle-aged men who are receiving maintenance levels of TRT versus men who are not receiving TRT.

$H_0$2: There was no difference in the level of anxiety experienced by middle-aged men who are receiving maintenance levels of TRT versus men who are not receiving TRT.

$H_1$2: There was a difference in the level of anxiety experienced by middle-aged men who are receiving maintenance levels of TRT versus men who are not receiving TRT.

$H_0$3: There was no difference in attention problems experienced by middle-aged men who are receiving maintenance levels of TRT versus men who are not receiving TRT.

$H_1$3: There was a difference in attention problems experienced by middle-aged men who are receiving maintenance levels of TRT versus men who are not receiving TRT.

Theoretical and Conceptual Framework for the Study

As early as the 1930s, medical practitioners/researchers noted an association between the male sex drive, erectile function, depression, memory issues, and fatigue (Heller & Myers, 1944; Hoberman & Yesalis, 1995). These early practitioners and researchers used TRT to address these concerns (Heller & Myers, 1944; Hoberman & Yesalis, 1995). The early clinicians saw in practice that their male patients benefitted from the use of TRT in these areas of medical concern (Heller & Myers, 1944; Hoberman & Yesalis, 1995). The use of TRT in this historical context set the stage for future research that looks beyond the sex-only early focus of the early 20th century to a broader focus that looks at how general medical conditions (e.g., diabetes mellitus II, obesity, metabolic syndrome [MetS], etc.) may impact testosterone levels in men of any age, and

how hypogonadism may affect mood in men as they move along the life span (Dunbar et al., 2008).

The theoretical method used by medical researchers was the biological model or biomedical model of psychological abnormality (citation). Users of this model assume that psychological disorders result from diseases or illnesses that affect the brain and/or nervous system (Abramowitz, 2015). Further, the biological model users asserted that biological health problems, such as changes in neurotransmitter levels, levels of certain hormones, or dysfunction of specific neurons in the brain, can result in negative impact on the psychological state of human beings (Abramowitz, 2015; Deacon, 2013). The researchers suggested that treatment for such abnormal psychological state of mind is best addressed with medications that correct the biological problem, which would in turn improve the psychological state of mind of the patient (Abramowitz, 2015).

With regard to testosterone levels in men, this theoretical model has been used in studies cited in Chapter 2 that sought to determine if there was an association or relationship between the testosterone levels in men, and the psychological distress (i.e., depression) experienced by men who have become hypogonadal (see Barrett-Connor, Von Mühlen, D., & Kritz-Silverstein, 1999; Emmelot-Vonk et al., 2008; Giltay et al., 2010; A. Gray, Feldman, McKinlay, & Longcope, 1991 Hintikka et al., 2009; Khera et al., 2012; Moffat et al., 2002; Wang et al., 2000; Wu et al., 2010).

Medical research studies cited in this study included examining the relationship between testosterone levels in men and their psychological state of mind and used psychometric instruments such as the Beck Depression Inventory (BDI), BDI-1A,

Hamilton, and the PHQ-9, which are self-report inventories that assist mental-health care practitioners in the diagnosis of depression (Barrett-Connor et al., 1999; Giltay et al., 2010; Khera et al., 2012). Medical researchers have also been concerned with what measures of testosterone levels, such as FT, BT, or total testosterone (TT), are the best predictors of changes in mood in men (Barrett-Connor et al., 1999; Giltay et al., 2010; Khera et al., 2012).

The conceptual framework for the present study begins with a discussion of what has variously been termed, and/or described, as andropause, male menopause, or *midlife crisis*. Other terms have been used for this phenomenon in the lives of many middle-aged men and men in late life. These terms were *viropause*, *male climeractic*, and *androclise* (Ferriman, 1995; Gould, Petty, & Jacobs, 2000; Heller & Myers, 1944; Solstad, & Garde, 1992; Vermeulen, 1993). The use of the aforementioned terms has served to support the notion that age-related symptoms men experience in midlife are analogous to menopause experienced by women. However, to make a claim such as this was to fundamentally misunderstand the biological and psychological changes occurring as women and men enter midlife (Newhart, 2013). According to Newhart (2013), menopause is not a singular event, but is a life transition that occurs over a 7–10-year period. What is commonly referred to as menopause is currently viewed as a threefold process that includes (a) perimenopause (sometimes referred to as *menopausal transition*, and has an average length of 4 years), (b) final menstrual period, and (c) postmenopause, which begins 12-months after the final menstrual period, and is usually divided into early and late postmenopause (Newhart, 2013). Terms such as male menopause, as well as the other

aforementioned terms, have led to the erroneous popular assumption that middle-aged men experience sharply declining hormone levels and concurrent symptomology (Boul, 2003; Charlton, 2004).

Within the medical research community, especially within the field of endocrinology, there has long been an interest in discovering the relationship, if any, between testosterone levels and depressed mood in men (P. B. Gray et al., 2005; Hintikka et al., 2009; Moffat et al, 2002; Rizvi et al., 2010; Wang et al., 2004; Wang et al., 2000; Wu et al., 2010). More specifically, medical researchers have sought to determine whether or not there is a causal relationship between testosterone levels in men, mood, and age. Much of the research over the past 15 years has sought to determine whether age-related decline in testosterone levels in men has a causal relationship with depressed mood (P. B. Gray et al., 2005; Hintikka et al., 2009; Moffat et al, 2002; Rizvi et al., 2010; Wang et al., 2004; Wang et al., 2000; Wu et al., 2010). The present study benefits from scholarly discussion, as it has helped to define what is largely missing from scholarly literature in general, which is that the relationship has been almost entirely studied from a medical perspective. Further, psychologists have been nearly silent on the subject in their studies, which will be discussed in greater detail in Chapter 2.

Nature of the Study

This was a quantitative study that used a psychological self-report inventory/survey designed to assess the psychological state of mind of respondents. The survey instrument used in this study was a psychological self-report inventory that measured the key variables of concern: depression, anxiety, and/or attention problems.

The independent variable used was middle-aged men on TRT at maintenance levels for at least 12 months. The dependent variables were depression, anxiety, or attention problems. The resulting data were analyzed using the multivariate analysis of variance (MANOVA).

Definition of Terms

Hypogonadism: Inadequate production of sex hormones, or low serum levels of sex hormones ("Hypogonadism," 2005).

*Late-on*set *hypogonadism (LOH)*: LOH is defined by reduced serum testosterone levels (either TT or FT) and the careful exclusion of any form of classical hypogonadism, and associated with advancing age (i.e., less than or equal to 65 years of age; Schubert & Jockenhövel, 2005).

Testosterone: The major androgenic hormone; it is responsible for the development of the male external genitalia and secondary sexual characteristics (citation). In females, its main role is as an estrogen precursor (citation). In both genders, it also exerts anabolic effects and influences behavior (Mayo Clinic Laboratories, n.d.).

Total testosterone(TT): The TT is testosterone that is bound to proteins in the blood (e.g., albumin and sex-hormone binding globulin [SHBG]) as well as FT; American Association for Clinical Chemistry, n.d.).

Serum, bioavailable, and free testosterone: These terms are roughly synonymous and used here interchangeably. These terms refer to most circulating testosterone. It is bound SHBG), which in men also is called testosterone-binding globulin. A lesser fraction is albumin bound and a small proportion exists as free hormone.

Historically, only the free testosterone was thought to be the biologically active component. However, testosterone is weakly bound to serum albumin and dissociates freely in the capillary bed, thereby becoming readily available for tissue uptake. All non-SHBG-bound testosterone is therefore considered bioavailable (Mayo Clinic Laboratories, n.d.).

Assumptions

1. I assumed that research participants would be honest in answering the questions on the Health Dynamics Inventory Self-Report (HDI–S)–. The veracity of patient answers on psychological self-inventories was assumed by clinicians.
2. I assumed that research participants in Group A had received testing that had determined their hypogonadal status, as would be required prior to his physician prescribing TRT.
3. It is possible that some research participants in Group B may have needed TRT, while others may not have. It was not feasible to determine which men in Group B needed or did not need TRT. Testing for testosterone levels in men was not part of routine health screenings for men and was not part scope of this study. The gonadal status of these men was unknown at the time of this study.

Scope and Delimitations

In this study, I was concerned with the psychological impact of TRT on middle-age men. My focus was whether TRT had an impact on middle-aged men who may

experience depression, anxiety, and/or attention problems. This is of principal concern to clinical psychologists, but should also be of interest to medical doctors, medical researchers, and other mental-health care clinicians. There was no study found in the psychology literature reviewed for this research study that sought to assess how men in middle-age who are recipients of TRT feel in relation to anxiety and/or attention problems versus those who are not recipients.

The primary boundary in this study was that the target population is middle-aged men between the ages of 45-64. The men selected for this study were a sample population of convenience, in that they were selected from among patients in four medical practices based in adjacent suburbs in northeastern Ohio.

The study sample was comprised of men between the ages of 45 and 64. This was a convenience sample and the population was not selected to suggest that men who are older or younger with hypogonadism do not potentially have mental-health concerns across the spectrum of mental-health issues. This study did not include men below the age of 45, or above the age of 64. Also, women and/or members of the transgender community were not included in the present study, as they may well receive other hormonal treatments, but as such, the findings of this study would not generalize to these populations.

Limitations

1. The population sample for the study was a sample of convenience.
2. I was not directly involved with research participants, or their selection. There was no assignment bias that influenced study outcomes.

3. This was the first study conducted in clinical psychology research to assess the impact of TRT in middle-aged men who may experience depression, anxiety, and/or attention problems. A self-report psychometric instrument was used to assess whether TRT had a psychological impact on middle-aged men.
4. In the control group (Group B) there was likely both men who need TRT and men who did not need TRT.

Significance

This study contributes to the scientific knowledge base in the field of psychology by its investigation of the relationship between TRT and mental-health issues among middle-aged men. Understanding the impact of TRT in this population as it relates to mental-health issues among middle-aged men could increase clinician capacity to reduce the negative impact mental-health issues can have in this population, and consequently increase the patient's positive experience of his own quality of life.

The study may advance mental-health practice, in that the routine examination of medical issues that can affect mood, such as thyroid issues, MetS, or diabetes, would come to include testing to determine if a middle-aged male patient experiencing depression, anxiety, and/or attention problems, is a candidate for TRT to aid in addressing his emotional distress.

The results of this study may impact how men around the world experience their psychological state of mind, insofar as depression, anxiety, and/or attention problems are concerned. This could potentially promote social change on an international level and thereby be life enhancing for countless men.

Summary

Many middle-aged men complain of increased depression, anxiety, and/or attention problems, which suggests a range of mental-health issues that may be related to hypogonadism. Although existing research does point to a relationship between hypogonadism and depression, there was no current research assessing the relationship between hypogonadism and other mental health issues, such as anxiety, and/or attention problems. I focused on the relationship between hypogonadism, TRT, and the mental-health issues described above. The results of this research provide valuable information about hypogonadism, TRT, and mental-health issues faced by middle-aged men, and how clinicians may best serve men who meet the *Diagnostic and Statistical Manual of Mental Disorders* (5th ed.; American Psychiatric Association, 2013) criteria for these mental-health concerns. It should be noted that the clinician, when assessing the middle-aged man's psychological concerns in relation to hypogonadism and other health concerns that can affect mood, should consider any one, or a combination, of these mental-health issues.

Chapter 2 provides the comprehensive literature review that includes literature search strategy, theoretical foundation, conceptual framework, and literature review related to key variables and/or concepts on hypogonadism, TRT, depression, and cognitive issues discussed in available scholarly research.

Chapter 2: Literature Review

Introduction

The problem addressed in this study was that as men move through the life span, many begin to experience or have an increased experience of mental-health issues such as depression, anxiety, and/or attention problems (see citation). The purpose of this study was to discover any clinically significant differences in depression, anxiety, and/or attention problems experienced by middle-aged men who received maintenance level doses of TRT versus middle-aged men who had not receive maintenance level doses of TRT. In this chapter I discuss the literature search strategy, theoretical foundation, conceptual foundation, and reviewed literature related to key variables.

Literature Search Strategy

A comprehensive literature review was completed over the course of 2 years (2014-2015) prior to the implementation of the present study. The databases used were PsycINFO, PsycARTICLES, and Psychology: A SAGE Full-Text Collection, as well as NIH/NIM Medline. The primary keywords and word combinations used were andropause, male menopause, male *midlife crisis*, male middle age, testosterone replacement therapy and mood, testosterone replacement therapy and depression, testosterone replacement therapy and sleep, testosterone replacement therapy and cognitive ability, testosterone replacement therapy and anxiety, and testosterone replacement therapy and life satisfaction. Other keywords and keyword combinations used were hormone replacement therapy and anxiety, hormone replacement therapy and mood, hormone replacement therapy and depression, hormone replacement therapy and

cognitive ability, hormone replacement therapy and sleep, and hormone replacement therapy and life satisfaction.

This literature review includes seminal literature from Wang et al. (2004), Wang et al. (2000), and Barrett-Connor et al. (1999). Current peer-reviewed literature reviewed and included for the present study was from Emmelot-Vonk et al. (2008), P. B. Gray et al. (2005), Hintikka et al. (2009), and Khera et al. (2012). As can be seen, there was precious little current research literature (including dissertations and/or conference proceedings) pertaining to TRT and depression, and/or other mood-related issues faced by men in middle age as it relates to TRT. The research available came from medical research, as little to no psychology research on the subject appears to have been published.

The dearth of research I found on the subject of the present study is a reason that the present study is significant and encouraged me to help close the research gap and try to discover whether TRT can assist some middle-aged men who face psychological distress resulting from hypogonadism. This study may provide some guidance to medical clinicians, such as psychiatrists, primary-care physicians, and endocrinologists, as well as clinical psychologists who see middle-aged men in their practice. This provides another avenue that may serve to connect medical practitioners with clinical psychologists so that their mutual patients may gain the greatest possible benefit from their discreet areas of health-care practice.

The theoretical method used by medical researchers was the biomedical model, which combines pharmacological treatment with psychological self-report inventories to

determine if there was an association or relationship between the testosterone levels in men, and the psychological distress experienced by some men who have become hypogonadal (Abramowitz, 2015). My study used the biomedical model of treating abnormal psychological conditions (Abramowitz, 2015). There are few, if any, current peer reviewed research studies conducted by researchers who are clinical psychologists. This literature review found no such studies.

Theoretical Foundation

As early as the 1930s, medical practitioners/researchers have noted an association between the male sex drive and erectile function (Hoberman, & Yesalis, 1995). These early practitioners/researchers used TRT to address these concerns (Hoberman, & Yesalis, 1995). Those early clinicians saw in practice that their male patients benefitted from the use of TRT in these areas of medical concern (Hoberman, & Yesalis, 1995). The use of TRT in this historical context set the stage for future research that looked beyond the sex-only related early focus of the early 20th century to a broader focus that looks at how general medical conditions (e.g., diabetes mellitus II, obesity, MetS, etc.) may impact testosterone levels in men of any age, and how hypogonadism may affect mood in men, as men move along the life span.

This study used the biomedical model of treating abnormal psychological conditions. This theoretical model combines pharmacological treatment with psychological self-report inventories to determine if there was an association or relationship between the testosterone levels in men, and the psychological distress experienced by men who have become hypogonadal (Barrett-Connor et al., 1999;

Emmelot-Vonk et al., 2008; Giltay et al., 2010; P. B. Gray et al., 2005; Hintikka et al., 2009; Khera et al., 2012; Moffat et al., 2002; Wang et al., 2004; Wang et al., 2000; Wu et al., 2010).

Research studies cited in this literature review used psychometric instruments such as the BDI, BDI-1A, and the PHQ-9, which are self-report inventories that assist mental-health care practitioners in the diagnosis of depression (Barrett-Connor et al., 1999; Giltay et al., 2010; Khera et al., 2012). Medical research had also been concerned with what measures of testosterone levels, such as FT, BT, or TT are the best predictors of changes in mood in men (citation).

My study used the HDI–S, which is a psychological self-report inventory, to assess the impact of TRT on depression, anxiety, and/or attention issues experience by middle-aged men.

Conceptual Framework

As stated previously, the conceptual framework for the present study began with a discussion of what has variously been termed, and/or described as *aging male syndrome*, andropause, male menopause, or *midlife crisis* (Boul, 2003; Charlton, 2004). Other terms have been used to describe this phenomenon in the lives of many middle-aged and late-life men. These terms are viropause, male climeractic, and androclise (Ferriman, 1995; Gould et al., 2000; Heller & Myers, 1944; Solstad & Garde, 1992; Vermeulen, 1993). The use of the aforementioned terms has served to support the notion that age-related symptoms men experience in midlife are analogous to menopause experienced by women.

Terms such as male menopause, as well as the other terms mentioned, have led to the erroneous popular assumption that middle age men experience sharply declining hormone levels and concurrent symptomology (Charlton, 2004; Newhart, 2013). However, men usually experience a gradual decline in male hormones, principally testosterone, over the course of decades (Charlton, 2004; Newhart, 2013). This sharply contrasts with menopause as experienced by most women, which occurs over a much shorter time frame, and usually around a woman's late 40s or early 50s (Charlton, 2004; Newhart, 2013).

Within the medical research community, especially within the field of endocrinology, there has long been an interest in discovering the relationship, if any, between testosterone levels and depressed mood in men (P. B. Gray et al., 2005; Hintikka et al., 2009; Moffat et al., 2002; Rizvi et al., 2010; Wang et al., 2004; Wang et al., 2000; Wu et al., 2010). More specifically, medical researchers have sought to determine whether or not there is a causal relationship between testosterone levels in men, mood, and age. Many of the researchers over the past 15 years sought to determine whether age-related decline in testosterone levels in men has a causal relationship with depressed mood (see citation). My study benefitted from scholarly discussion in that the discussion helped me to define my study and to be sure that I would be making an original research contribution to the field.

Literature Review Related to Key Variables

The relationship between decreasing levels of testosterone in men as they age, hypogonadism, and LOH has been, and continues to be, the subject of some debate and

controversy (Emmelot-Vonk et al., 2008), although the most current literature seems far less the subject of debate or controversy, as the positive effects of TRT on mood in men appear to have become more accepted. Emmelot-Vonk et al. (2008) postulated that the mixed findings found among previous studies are likely due to differences in study designs, including such things as the age of research participants, gonadal status, research participant general-health status, method of treatment administration, duration of treatment, instrumentation used to study aging, and/or laboratory methods used to assess testosterone levels in male research participants.

The scholarly research available focused on the relationship of testosterone levels in men to men's experience of depression, although some of the same literature makes mention of testosterone levels being related to other mental-health issues faced by men as they move along the life span. Such issues included, but were not limited to, depression, anxiety, sleep disturbance, and/or attention problems (Khera et al., 2012). The measures of psychological distress chosen for the present study were depression, anxiety, and/or attention problems.

Wu et al. (2010) surveyed a random sampling of men age 40 to 79, with a mean age of 59. The sample population was comprised of 3,369 men randomly selected from among eight European locations (Wu et al., 2010). The aim of the study was to determine whether there was a relationship between morning blood samples examined by mass spectrometry, and Vermeulen's formula that measures FT (Wu et al., 2010). Further, of particular interest to the study's authors was the relationship, if any, between symptoms of poor morning erection, libido, erectile function, and ability to engage in vigorous

activity, depression, and energy level (Wu et al., 2010). The survey instrument used to examine depressed mood for the study was the BDI. Within the context of mood, or more specifically depression, the researcher's interest was primarily focused on energy level (i.e., loss of energy), sadness, and fatigue (Wu et al., 2010). Wu et al. (2010) concluded that the depression symptoms examined had little or no relation with men's testosterone level. The authors acknowledged that these findings support the results of some studies (e.g., Delhez, Hansenne, & Legros, 2003; Tancredi et al., 2004), but contradict the findings of other studies (Bhasin et al., 2010; P. B. Gray et al., 2005; Zitzmann, Faber, & Nieschlag, 2006) . However, the authors also concluded that there may be many different testosterone levels or thresholds that may exist for various levels of hypogonadism among men in middle and late life (Bhasin et al., 2010 P. B. Gray et al., 2005; Zitzmann et al., 2006). These researchers' findings are not supported by the findings of other research studies. Because there is still some debate about the effectiveness and efficacy of TRT on depression, I set out to verify the actuality.

Giltay et al. (2010) completed a randomized, double-blind, 30-week clinical trial of testosterone undecanoate (TU), with placebo control, of 184 urban Russian men. The mean age of these men was 52.1 years, ranging from age 35-69 (Giltay et al., 2010). The study was conducted from October 2005 through October 2008 (Giltay et al., 2010). The authors acknowledged that testosterone levels in men progressively diminish with increasing age (Giltay et al., 2010). As it related to the psychological state of men in mid and late life, the authors further postulated that low testosterone levels in men can be associated with symptoms including dysphoria, diminishing vitality, and irritability

(Giltay et al., 2010). Also, the authors asserted that depression may negatively impact sexual function in men, including such symptoms as erectile dysfunction, decreased libido, and orgasm (Barrett-Connor et al., 1999; Rizvi et al., 2010; Seidman, Araujo, Roose, & McKinlay, 2001; Wang et al., 2009). The authors noted that in instances where men are deprived of TRT, perhaps being due to treatment for prostate cancer, such men have been noted as having increased occurrences of anxiety, lack of energy (i.e., fatigue), decreased drive, and lethargy (Almeida, Waterreus, Spry, Flicker, & Martins, 2004; Shahinian, Kuo, Freeman, & Goodwin, 2006). The researchers noted that elderly men with the syndrome associated with hypogonadism is often referred to as LOH, or testosterone-deficiency syndrome of the aging male (Tenover, 1992). The authors emphasized that there is a substantial overlap in the occurrence of hypogonadism and depressive symptoms seen in men in middle and late life (Almeida et al., 2004; Shahinian et al., 2006). Further, the relationship between TT and FT levels in middle-aged and elderly men demonstrate an inverse and independent relationship to depressive symptoms (Barrett-Connor et al., 1999; Zitzmann et al., 2006). The studies discussed here suggested that middle-aged men and men in late life may suffer from the same symptomology resulting from hypogonadism.

The aim of a study by Giltay et al. (2010) was to determine whether TRT would significantly decrease symptoms of depression and aging-male symptoms such as MetS, with each research participant being overweight or obese at baseline, and alternatively to improve sexual function to a significant extent. MetS may place a man at increased risk of Type II diabetes mellitus and cardiovascular disease (Alberti, Zimmet, & Shaw, 2005).

Also, MetS may place men at increased risk for hypogonadism and depressive symptoms (Akbaraly et al., 2009; Dunbar et al., 2008; Koponen, Jokelainen, Keinanen-Kiukaanniemi, Kumpusalo, & Vanhala, 2008; Skilton, Moulin, Terra, & Bonnet, 2007).Giltay et al. (2010) used the BDI-1A to measure depression, comparing changes that occurred between men receiving TU versus the placebo group. Direct comparison of these levels at baseline, 18 weeks, and 30 weeks, showed significant improvements in BDI-1A scores (Giltay et al., 2010). In the TU group, 59.3%, or 67 of 113 men had scores that indicated moderate to severe depression on the BDI-1A at baseline (citation). At 18 weeks of treatment with TU, the number of men reporting depressive symptoms, as measured by the BDI-1A, decreased to 39.8%, or 43 of 113 men (Giltay et al., 2010). At 30 weeks of treatment with TU, the number of men reporting depressive symptoms, as measured by the BDI-1A had further decreased 235.2%, or 37 of 113 men (Giltay et al., 2010).

Changes among men assigned to the placebo group were minimal (Giltay et al., 2010). Posthoc analysis revealed that the greatest effect on men for depressive symptoms was among those with the lowest total and BT levels at baseline (Giltay et al., 2010). Researchers also found that there was a significant change in the body mass index of research participants who sections used TU. For the males receiving TU, there was an average decrease in body mass index of -1.32 kg/m^2, and an insignificant change of –0.11 kg/m^2 among research participants in the placebo group (citation). This study demonstrated that the worse a man's hypogonadism the better his state of mind, which could help other physiological factors to improve.

Hintikka et al. (2009) performed an examination of responses from 116 middle-aged men to a health questionnaire that was mailed to them. The questionnaires were mailed in 1998 (N = 3,040 and final N = 2,050), with follow-ups performed in 1999 (N = 1,722), and 2001 (N = 1,347; Hintikka et al., 2009). These questionnaires were sent to a population-based sample taken from the national population register. The data came from a total random sample of 2,050 Finnish men (Hintikka et al., 2009). Of these large random samples taken from Finnish men, 116 middle-aged men were selected in 2005 for clinical examination to facilitate research efforts to determine the associations, if any, between long-term symptoms of decreased depression and circulating testosterone levels in middle-aged men (Hintikka et al., 2009). The latter-most group was selected due to having reported depression (Hintikka et al., 2009. The BDI-21, and the Hamilton Depression Rating Scale were the psychometric instruments used to assess depression (Hintikka et al., 2009).

Hintikka et al. (2009) began their research study noting that research estimated that the FT levels of men between the ages of 40–70 decreases by 1.2% annually (see A. Gray et al., 1991; Lunenfeld, 2006). These researchers also found that approximately 80% of testosterone is bound primarily to SHBG, which increases 1.2% annually in this age group. As SHBG increases, active FT tends to decrease (Lund, Bever-Stille, & Perry, 1999). Hintikka et al. (2009) pointed out that other factors that can cause FT levels to decline are medical conditions, obesity, and alcohol abuse. The effects of low levels of circulating FT have been associated with symptoms of depression, anxiety, irritability, and hyposomnia (Almeida, Yeap, Hankey, Jamrozik, & Flicker, 2008; Barrett-Connor et

al., 1999; Perry et al., 2001; Sternbach, 1998). The 2-year occurrence of depression in men aged 45 and older was 21.7% among hypogonadal men, as contrasted with 7.1% of eugonadal men (Shores et al., 2004). Hintikka et al. (2009) acknowledged that although there are studies with data that both supports and refutes an association between testosterone and depression in middle-aged men, and men in late life, the connection between testosterone levels and depression continued to be hotly debated and controversial among medical research scholars (Carnahan & Perry, 2004; Seidman et al., 2001).

Hintikka et al. (2009) found that hypogonadism among research participants in this study was present in 19.8% of men and was associated with clinically significant depression as reflected by their BDI-21 scores. Clinically significant depression was more common within the group of men with hypogonadism. Study results showed that 34.8% of men with hypogonadism had symptoms of clinically significant depression versus 9.7% of other men (Hintikka et al., 2009). Based on their findings, the researchers found that among middle-aged men who showed clinically significant depression, as well as men who had long-term depressive symptoms, also had hypogonadism (Hintikka et al., 2009). The researchers noted that decreased libido was also common among men with hypogonadism. However, the researchers also noted that though decreased libido was common among men with hypogonadism, decreased libido is associated with clinically significant depression regardless of whether the man has hypogonadism or not (Hintikka et al., 2009). The researchers concluded that while decreased libido can be a symptom of

depression, their research also suggests that hypogonadism may well be a significant factor related to depression among middle-aged men (Hintikka et al., 2009).

A seminal research study conducted by Wang et al. (2000) compared the impact of transdermal testosterone gel versus testosterone patch administration to men. The aim of their study was to assess whether there was a difference in the extent to which, if any, the method of administration may have had in men related to their sexual motivation, sexual performance, overall sexual desire, sexual enjoyment (with intimate partner), erection satisfaction, erection percent, positive mood, negative mood, leg strength, arm strength, total body mass, fat mass, lean mass, and percent of body mass.

Wang et al. (2000) recruited and studied research participants in 16 locations across the United States. Research participants were hypogonadal men between the ages of 19 and 68. Research participants in this study, although hypogonadal, were otherwise generally in good health, with normal prostate-specific antigen (PSA) levels (Wang et al., 2000). There were 227 research participants who took part in this study. Research participants were randomized into three groups comprised of 73 men, 78 men, and 76 men. The three groups received gel dosed in 50 mg per day of testosterone administered in 5 g of testosterone gel, 100 mg per day of testosterone gel administered, and 10 g of testosterone gel, or two nonscrotal patches that administer 5 mg per day, respectively (Wang et al., 2000). Research participants were clinically assessed at baseline (i.e., 0 days), 30, 60, 90, 120, 150, and 180 day intervals (Wang et al., 2000). Clinical assessment included fasting blood samples, hematology and clinical biochemistry,

electrolytes, glucose, kidney and liver function, lipid profile, and mood (Wang et al., 2000).

Wang et al.'s (2000) research findings showed no clinically significant decrease in the testosterone patch group for fat mass or percent fat; however, there were clinically significant decreases in fat mass and percent fat within the testosterone gel groups (Wang et al., 2000). Also, there were clinically significant increases in lean mass and decreases in fat mass that were correlated with changes in the mean serum testosterone levels achieved after the administration of testosterone gel replacement (Wang et al., 2000). The beneficial effects and increased efficacy with the use of testosterone gel were accompanied by increases in the hematocrit and hemoglobin levels, but PSA levels remained in the normal range as did research participant lipid profiles (Wang et al., 2000). Researchers noted that the greatest clinically significant increases occurring in the study were in the group that received the 100 mg per day treatment with the testosterone gel (Wang et al., 2000).

As it related to the Wang et al. (2000) study, mood was assessed using a 0–7 Likert-style scale that measured positive mood responses that included *feeling alert*, *outgoing*, *energetic*, *feeling well overall*, and *a general sense of well-being*. Negative mood responses included feelings such as *anger*, *irritability*, *sadness*, *fatigue*, and *nervousness*.

Wang and her colleagues (2000) concluded, in their seminal study, that testosterone gel replacement improved sexual function, mood, increased lean mass, increased muscle strength, and decreased fat mass in hypogonadal research participants.

Another benefit of treatment with testosterone gel noted in this research study was that there was less skin irritation and patient discontinuation of treatment with testosterone gel versus the testosterone patch (Wang et al., 2000).

Wang et al. (2004) published a follow-up study that extended the research done in Wang et al. (2000). The aim of this study was to examine whether gains in serum testosterone levels, efficacy, and safety remained constant throughout the long-term use of testosterone gel in hypogonadal men. There were 163 hypogonadal men who participated in this research study. The specific testosterone gel used in this research study was AndroGel 1%. Research participants ranged in age between 19 and 68 years of age. Of the original 163 hypogonadal men who agreed to participate in this research study, 150 hypogonadal men participated throughout the entirety of the study. Aside from being hypogonadal, each of the men participating in the study was generally in good health, which was determined by previous medical history, physical examination, and blood count, which included serum testosterone levels. Research participants had no history of chronic illness or disease, alcohol, or substance abuse. Additionally, PSA levels were normal, as was digital rectal examination of the prostate.

Wang et al. (2004) looked at sexual function, mood, body composition, bone turnover markers, hemoglobin, hematocrit, serum PSA levels, and prostate disease. Wang and her colleagues (2004) found that with 6 months of TRT there was significant improvement in sexual function, mood, lean mass, and in muscle strength. They also found were decreases and fat mass, and the percent of body fat. With regard to bone turnover markers, there was an inconsistent increase in bone-formation markers, but more

sustained decreases in bone resorption markers. Research participants received testosterone replacement gel with 5, 7.5, or 10 g doses of testosterone gel 1% (e.g., AndroGel 1%). Research participants receiving AndroGel 1% with 10 g doses testosterone saw a 2% increase in bone mineral density in the vertebrae by 6 months (Swerdloff et al., 2000).

With specific regard to mood, Wang and her colleagues (2004) found that positive mood scores improved with treatment and was sustained over the course of treatment; whereas negative mood scores decreased and remained significantly lower than at baseline with sustained treatment after 6 months of testosterone replacement. Wang and her colleagues (2004) used the same mood parameters in this research study as was used in Wang et al. (2000).

Barrett-Conner et al. (1999) examined 856 men ages 50 to 89 who had attended a community clinic between 1984 and 1987. The aim of this study was to determine whether plasma testosterone levels were related to depressed mood or categorical depression in these 856 community-dwelling older men. The 856 men reported in the study had originally been research participants between 1972 and 1974 in which they were assessed for risk factors related to heart disease (Barrett-Connor et al., 1999). During the period between 1984 and 1987, surviving members of the original study participated in further research to study diabetes. This study assessed information gathered from research participants, including physical activity level, current lifestyle, cigarette smoking, and the extent of regular alcohol consumption, as well as height, weight, and hip and waist circumference. Information regarding depressed mood among

research participants was gathered using the BDI (Barrett-Connor et al., 1999). The study assessed levels of BT, bioavailable estradiols, as well as dihydrotestosterone levels (Barrett-Connor et al., 1999).

Barrett-Conner et al. (1999) found clinically significant and inversely associated with BDI scores and BT, and similar associations were found between BDI scores and dihydrotestosterone levels. These finding were independent of age, change in weight, and level of physical activity. Study findings showed that BT levels were 17% lower for 25 research participants who had categorically defined depression compared to levels observed in all other research participants (Barrett-Connor et al., 1999). Estradiols, total or bioavailable, were not associated with depressed mood. The researchers concluded that testosterone treatment might lessen depressed mood among older men who have low BT levels (Barrett-Connor et al., 1999). These researchers acknowledged that their findings confirm the findings of other research studies, and conflict with others, so from their perspective the topic remains controversial among medical researchers concerned with this area of research (Barrett-Connor et al., 1999).

Moffat et al. (2002) examined 407 men, aged 50 to 91. Research participants were from the Baltimore Longitudinal Study of Aging. The researchers in this study sought to determine if there were any age-related decreases in TT or FT, and declines in neuropsychological ability. Research participants were followed for an average of 10 years, during which they were assessed from multiple cognitive domains with concurrent determination of TT and FT levels (Moffat et al., 2002). The researchers administered neuropsychological psychometric tests that measured verbal and visual memory, mental

status, visuomotor scanning and attention, verbal knowledge and language, visuospatial ability, and depressive symptomology (Moffat et al., 2002).

Moffat et al. (2002) noted that the late life span in human beings is punctuated with declines in physiological function, including some aspects of cognitive performance for men. The researchers also noted that such age-related declines in cognitive performance, as well as the factors that contribute to it, have not been well-characterized or documented (Moffat et al., 2002). Of particular interest to these researchers was recent evidence, which suggested that the human males' endocrine environment might moderate cognitive declines in older men (Moffat et al., 2002). The authors pointed out that TT levels in men may decline as much as 50% from ages 30 to 80, and as many as 68% of men over the age of 70 may be classified as hypogonadal based on their FT levels (Moffat et al., 2002).

Moffat et al. (2002) reported that there have been very few studies conducted that have explored the relationship between T and cognitive performance in older men. One such study, Barrett-Conner et al. (1999), examined the association between baseline T and cognitive performance in 547 men ages 59 to 89 (Barrett-Connor et al., 1999). The researchers in that study found that men who scored better on a measure of long-term verbal memory also had higher concentrations of BT than men with lower concentrations of BT (Barrett-Connor et al., 1999). Two other studies conducted showed an improvement in visuospatial performance in older men who received testosterone supplementation (Cherrier et al., 2001; Janowsky, Oviatt, & Orwoll, 1994), a third study showed improved performance in verbal memory (Cherrier et al., 2002), and a fourth

study reported an improvement in working memory (Janowsky, Chavez, & Orwoll, 2000). It should be noted that in each of these studies, including the present study, research participants were men without dementia (Cherrier et al., 2002; Janowsky et al., 2000). It should be noted that in my study, volunteer research participants who met the criteria for probable or possible Alzheimer's disease, Parkinson's disease, cerebral vascular disease, other unspecified dementias, and cancer patients were excluded..

Moffat et al. (2002) reported that research participants classified as being hypogonadal had lower scores on cognitive status measures, including measures of visual memory, immediate verbal memory, delayed verbal memory, visuospatial rotation, as well as visuomotor scanning. On the other hand, mental status, verbal knowledge, and symptoms of depression did not demonstrate a statistically significant difference between hypogonadal and eugonadal research participants (Moffat et al., 2002). This study also showed FT to be a better predictor of cognitive performance for older men without dementia than did total T levels (Moffat et al., 2002). Additionally, FT was reported to be a more accurate predictor of true bioavailable T than is total T levels in men (Vermeulen, Verdonck, & Kaufman, 1999).

P. B. Gray et al. (2005) conducted a randomized study of 60 men aged 60 to 75 years. These researchers sought to determine if testosterone dose affects visuospatial cognition, sexual function, or mood. Specifically, these researchers examined the effects of graded testosterone-dose levels on visuospatial cognition, sexual function, depression or mania (P. B. Gray et al., 2005). The male research participants selected for this study were healthy men who were given monthly injections of a long-acting GnRH antagonist

(P. B. Gray et al., 2005). This antagonist was used to suppress endogenous production of testosterone. In addition, weekly injections of 1 of 5 different levels of testosterone enanthate were administered to each research participant corresponding with the dose group of which they were a part. Among the research participants, 13 men received doses 25 mg of the antagonist used to suppress their testosterone levels, 12 men received 50 mg, 12 men received 125 mg, 14 men received 300 mg, and 10 men received doses of 600 mg (P. B. Gray et al., 2005). Of the 52-research participants who completed treatment within the study, 44 of these men also completed questionnaires on sexual function and mood (P. B. Gray et al., 2005). Men with BPH, history of prostate cancer, PSA reading of 4 ng/ml or higher, Type II diabetes, or a history of heart attack or congestive heart failure within the prior 6-month period were excluded from participation in this study (P. B. Gray et al., 2005). Men were also excluded who were current participants in competitive sports, resistance training, or endurance training, as well as men receiving androgen-related steroids, growth hormone, or four anabolic steroids within the prior 12-month period (P. B. Gray et al., 2005).

In this study, P. B. Gray et al. (2005) found that among healthy older men, testosterone-dose response relationships for a number of domains of sexual function, as well as visuospatial cognition, differ between older and younger men. These researchers concluded, in this regard, that it may be inappropriate to extrapolate the effects of testosterone supplementation in younger men to that of older men, or vice versa (P. B. Gray et al., 2005). The data gathered by these researchers showed that testosterone supplementation can have positive effects on sexual function in older men (P. B. Gray et

al., 2005). Testosterone supplementation increased libido in research participants, and sexual activity depending upon whether or not the older man had an available sexual partner (P. B. Gray et al., 2005). This finding is consistent with previous studies that have examined the effects of testosterone interventions on sexual function. This study also found that testosterone is more closely related to the speed of information-processing responsiveness in older men than it is to spatial cognition and accuracy (Hooven, Chabris, Ellison, & Kosslyn, 2004). The researchers did not investigate improvement in verbal memory; however, they did note that testosterone supplementation has been shown to improve verbal memory (Cherrier et al., 2002). The findings of this research study did not show an impact from the testosterone supplementation on mood; however, the researchers noted that if the research-participant pool had included hypogonadal men, there would likely have been demonstrations of elevation of positive mood and/or decreases in depression that would have emerged (P. B. Gray et al., 2005; O'Connor, Archer, Hair, & Wu, 2001).

Emmelot-Vonk et al. (2008) conducted a study of older men to determine whether TRT could mediate the effects of aging. The specific effects of aging examined were functional mobility, cognitive function, bone mineral density, body composition, lipids, quality of life, and safety parameters (Emmelot-Vonk et al., 2008). Research participants where men aged 60 to 80 with low-normal testosterone levels. The researchers noted that among existing clinical trials conducted on older men, the effects of testosterone supplementation have provided mixed findings (see Sih et al., 1997; Snyder et al., 1999; Tenover, 1992). The researchers postulated that these mixed findings were likely due to

differences in research-study designs, including such things as the age of research participants, gonadal status, and research-participant overall health, as well as the method of administration, duration of treatment, and instrumentation used to study aging (Emmelot-Vonk et al., 2008). The researchers also noted that findings from these studies were difficult to generalize, as small sample sizes limited the statistical power to detect effects (Emmelot-Vonk et al., 2008).

The Emmelot-Vonk et al. (2008) study design was a randomized, double-blind, placebo-controlled design that included 237 men, aged 60 to 80, with testosterone levels lower than 13.7 nmol/L. The research participants were men from the Netherlands, which was conducted at a university medical center in the Netherlands (Emmelot-Vonk et al., 2008). Research participants were randomly designated to receive 80 mg of testosterone undecenoate or matching placebo, which were administered twice a day for a period of 6 months (Emmelot-Vonk et al., 2008).

Emmelot-Vonk et al. (2008) found that the administration (i.e., orally administered) of 80 mg of testosterone undecenoate twice daily to men with low-normal serum-testosterone levels increased lean body mass, and decreased fat mass; however, no improvement in functional mobility or muscle strength was found. The reduction in fat mass was accompanied by a decrease in HDL and total cholesterol (Emmelot-Vonk et al., 2008). Reduction in fat mass was also accompanied by a decrease in glucose level and an increase in insulin sensitivity (Emmelot-Vonk et al., 2008). No changes in cognitive function or bone mineral density were reported (Emmelot-Vonk et al., 2008). Also, no effects on prostate safety were found (Emmelot-Vonk et al., 2008).

Khera et al. (2012) conducted a study to determine what, if any, long-term effect TRT would have on the psychological state of mind of men with decreased testosterone levels, who were experiencing depression. These researchers noted that the most often experienced psychological health concern human beings may face over the course of a lifetime is depression (see Kessler et al., 2005). Women suffer depression at higher rates than men, but the difference disappears after age 65 (see Almeida et al., 2008) and it is not unusual for depression symptoms to be found in middle-aged, as well as elderly, men (see Bhasin et al., 2010). Symptoms experienced by middle-aged and elderly men include such symptoms as decreased libido, erectile dysfunction, sleep disturbance, and reduced physical performance, which are associated with hypogonadism or with a deficiency in testosterone (see Bhasin et al., 2010).

Khera et al. (2012) further noted that levels of testosterone begin to decrease in men after age 30 by about 1% annually (see Harman, Metter, Tobin, Pearson, Blackman, 2001). Men with hypogonadism will have a medical history that includes evidence of specific levels of decrease of total and FT (see AACE Hypogonadism Task Force, 2002; Arver & Lehtihet, 2009; Carnegie, 2004; O'Leary, 2003; Wang et al., 2009), as well as a diagnosis of hypogonadism with presenting issues including, but not limited to, erectile dysfunction, diminished libido, attention problems, problems with memory, problems with fatigue/decreased energy levels, and depressed mood (see Kanayama, Amiaz, Seidman, & Pope, 2007; O'Leary, 2003; Rhoden & Morgentaler, 2004;Wang et al., 2009). The researchers acknowledged that some studies have shown that TRT can bring relief for symptoms of depression associated with hypogonadism (see Löwe, Schenkel,

Carney-Doebbeling, & Göebel, 2006; Pope, Cohane, Kanayama, Siegel, & Hudson, 2003; Zarrouf, Artz, Griffith, Sirbu, & Kommor, 2009). But what remained unclear is whether TRT could be beneficial in treating an array of symptoms a patient might present with, such as some combination of those mentioned above. The specific aim of my study was to examine if hypogonadism was the cause of clinically significant symptoms of depression, anxiety, and attention issues with a considerable sample size of men with low testosterone levels. Also, whether TRT administered for a period of at least 1 year showed clinically significant improvement in these symptoms.

In the study conducted by Khera et al. (2012), TT, FT, or BT were used as measures to determine starting points for research participants, and then used again at 3-, 6-, and 9-month intervals. The PHQ-9, a self-report psychometric instrument that measures severity of depression symptoms was also administered as a starting point. It was also administered at 3-, 6-, and 9-month interval visits for monitoring purposes (Khera et al., 2012). Clinically significant improvement in research participant symptoms of depression symptoms was determined by reduced symptom scores as reflected through retest administration of the PHQ-9 (Khera et al., 2012).

According to Khera et al. (2012), in this large-scale study, symptoms of depression, as determined by administration of the PHQ-9, were found in 92.4% of research participants. Research-participants symptoms of depression comprised over 17% of the total population. Subcohorts of research participants who used medication were less than the age of 60, had low levels of TT, and clinically significant symptoms of depression showed a clinically significant decrease from over 17% to approximately 2%

as reflected by improved PHQ-9 scores (Khera et al., 2012). According to these researchers, after 12 months of TRT, the average decrease in PHQ-9 research-participant depression symptom scores was 5.62 plus or minus 6.24, which constitutes significant improvement (see Wittkampf et al., 2009). Subcohorts of research participants below the age of 60 and using antidepressant medication also showed decreases in depression-symptom scores of less than or equal to 5 points and showed clinically significant improvement with 12 months of treatment with TRT (Khera et al., 2012).

Khera et al. (2012) noted that, in general, clinically significant symptoms of depression are considered to be symptomatic of low levels of BT (see Kroenke, Spitzer, & Williams, 2001). Also noted by these researchers is that few large-scale epidemiological studies have identified a relationship between clinically significant depression and hypogonadism (Khera et al., 2012). Other researchers have determined clinically significant symptoms of depression a significant association with BT (see Miner, Khera, Bhattacharya, Blick, & Kushner, 2011), or with low FT/BT levels (Löwe, Unützer, Callahan, Perkins, & Kroenke, 2004). Two other studies found no association in the general population between depression symptoms and testosterone levels (Barrett-Connor et al., 1999). However, according to Barrett-Connor et al. (1999), smaller studies have produced evidence linking depression symptoms and low testosterone levels (see Wu et al., 2010), and demonstrating that low testosterone in men was predictive of the likelihood they would have or would develop clinically significant of depression (see Araujo, Durante, Feldman, Goldstein, & McKinlay, 1998).

Similarly, Khera et al. (2012) found that PHQ-9 depression scores among research participants were not correlated with testosterone levels at the beginning of the study. Research participants with the severest clinically significant symptoms of depression also had severely low levels of testosterone (Khera et al., 2012). Research participants with higher levels of testosterone had improved depression scores (Khera et al., 2012). The researchers noted that while some studies have evidenced significant improvements in depression symptoms after 4 to 6 weeks of TRT, other studies, including this study (Khera et al., 2012), have shown that maximal improvement in depression symptoms may only be achieved after 6 to 12 months on TRT. The researchers also noted that differences in the length of time of TRT administration may differ from one individual to another, as no two individuals will necessarily respond within precisely the same timelines (Khera et al., 2012). Finally, the researchers concluded that TRT can serve to relieve depression symptoms experienced by hypogonadal patients (Khera et al., 2012). However, since no placebo was used in this study, the researchers were unable to draw any conclusions as to whether TRT treats depression as an illness (Khera et al., 2012).

Summary and Conclusions

There is a long history that spans nearly 90-years during which medical practitioners have treated men experiencing issues related to their sex lives using TRT (Hoberman, & Yesalis, 1995). During more recent decades, medical research scholars have shown increased interest in knowing whether or not TRT may be valuable in addressing other health or mental-health issues men may face as they move along the life

span (Hoberman, & Yesalis, 1995). The majority of the recent heightened research interest, and study implementation has focused on the TRT levels of decrease at which men may experience depression or other neurocognitive deficits (Swerdloff et al., 2000).

Reference has been made to psychological health issues, beyond depression, experienced by men in middle age and late life, as well as the likelihood that TRT may provide relief to their psychological distress (Charlton, 2004). However, when such mention has been made, there were no data to support the mention, although these mentions may be well founded (Charlton, 2004). What is known in relation to this study is that there is an inverse relationship between FT/BT and depression, energy level/fatigue, sadness, irritability, and insomnia (Khera et al., 2012). It is also known that testosterone supplementation can improve the positive aspects of mood and decrease the negative aspects of mood (see Kanayama et al., 2007; O'Leary, 2003; Rhoden & Morgentaler, 2004; Wang et al., 2009).

This literature review has shown that the method of administration used can help to ensure the maximum benefit to be derived from testosterone supplementation. Specifically, the beneficial impact of testosterone supplementation administration via transdermal gel applied daily has been found to greatly surpass that of transdermal patches (Wang et al., 2000).

As stated previously, the scholarly research currently available focused on the relationship of testosterone level in men to men's experience of depression, although some of the same literature makes mention of testosterone levels being related to other mental-health issues face by men as they move along the life span. Such issues included,

but were not limited to, anxiety and attention (Khera et al., 2012). These matters are particularly relevant for clinical psychologists. So, the measures of psychological distress selected for this study were depression, anxiety, and attention issues.

This study contributes to the scientific knowledge base in the field of psychology by its investigation of the relationship between TRT and mental-health issues often faced by middle-aged men. Understanding the impact of TRT in this population as it relates to mental-health issues among middle-aged men may increase clinician capacity to reduce the negative impact mental-health issues can have in this population while increasing the patient's positive aspects of mood and their consequent experience of their own quality of life.

Chapter 3 will present this study's research design, rationale, and methodology, which includes sampling and sampling procedures, as well as procedures for recruitment, participation, and data collection.

Chapter 3: Research Method

Introduction

The purpose of this study was to discover any clinically significant differences in the levels of depression, anxiety, or problems with attention experienced by middle-aged men who receive maintenance-level doses of TRT (i.e., receiving TRT for at least 12 months) versus middle-aged men who do not receive TRT. This chapter describes the research design and rationale, sample and population, instrumentation and materials, data collection, and analysis procedures.

Research Design and Rationale

This quantitative study was undertaken to determine if there was a difference in the levels of depression, anxiety, or attention problems experienced by middle-aged men in relation to testosterone levels. The dependent variables for this study were depression, anxiety, and attention problems. The independent variable was treatment with TRT. As seen in Chapter 2, studies have shown that as men move through life span, the male testosterone level decreases by 1% per year starting in the late 20s (Rizvi et al., 2010). Although not all researchers agree, there was evidence to suggest that TRT may have a positive impact that served to help mitigate or lessen psychological distress experienced by some middle-aged men (see citation). The HDI–S was used to assess the dependent variables in this study: depression, anxiety, and/or attention problems.

Methodology

Sampling and Sampling Procedures

The study sample consisted of a total of 180 middle-aged men aged 45-64. There were 90 middle-aged men aged 45-64 (Group A) who had been placed on TRT for at least 12 months, and 90 middle-aged men (Group B) who had never received TRT. According to the U.S. Census conducted in 2010, there were 39,743,507 men aged 45-64 residing in the United States (U.S. Census Bureau, 2010). Research participants for this study resided in suburbs of Northeastern Ohio. Research participants were patients of three area urologists who specialized in treating hypogonadal men using TRT (Group A), and a primary-care physician for collecting data from research participants who were part of the nontreatment group (Group B), which was from where the nontreatment group of research participants were accessed.

Sample Size

The power analysis conducted to determine the sample size for the present study determined that adequate power could be obtained with a total of 180 research participants, with 90 research participants in each of the two study groups. In order to calculate the sample size needed for this study, the power calculator G*Power was used (see Faul, Erdfelder, Buchner, & Lang, 2008). The parameters for calculating sample size were based on the MANOVA that was used in the study. Considering a medium effect size of .06, a generally accepted power of .80, and an alpha (α) significance level of .05, the desired sample size to achieve adequate power for a MANOVA is a total of 180 participants.

Procedures for Recruitment, Participation, and Data Collection

Permission to conduct this study this was obtained from Walden University's Institutional Review Board (IRB). A descriptive notice was developed and submitted for approval by the IRB describing the study, which was disseminated to each research participant. Research participants for this study was a sample of convenience drawn from the patients of three area urologists, and a primary-care physician. The sample from the urologists was comprised of middle-aged men who were receiving TRT and the sample of men who were not receiving TRT came from the patients of the primary-care physician. The descriptive notice included participant instructions for correct completion of the HDI–S. The descriptive notice also included information as to how I could be contacted in the event research participants had questions about the research that were not within the scope of the descriptive notice. The two tasks required to participate in this study were

1. Study-related questions from the potential volunteer research participants were encouraged and answered.
2. All participants were required to speak and read English, as the HDI is only available in English.

Instrumentation and Operationalization of Constructs

The instrumentation used is described below. The instrument used was a self-report inventory that was completed anonymously by each research participant, collected, and secured.

The HDI-S was selected for the present study, as it measures each of the variables

of concern in brief format. The HDI-S was released in 2012 (Saunders & Wojcik, 2003). The normative sample for the HDI included 2,161 patients and 1,574 outpatients. The HDI-S is an individually administered psychometric instrument developed as a quick and accurate means of measuring the current mental health status of individuals who are ages 18 and older (Saunders & Wojcik, 2003). The HDI-S was designed for use with new patients as well as being a tool to assess progress being made in treatment with continuing patients (Saunders & Wojcik, 2003). The HDI-S uses a background questionnaire to gather demographic, medical, and psychiatric history, as well as treatment experience and the reason for which the patient is seeking psychological treatment (Saunders & Wojcik, 2003).

The HDI-S was developed to measure three aspects of mental health, which are based on the tripartite mental-health model (Strupp & Hadley, 1977) and are as follows: (a) morale–measures the patient's level of emotional distress and sense of wellbeing and happiness; and (b) global symptom scale–measures patient levels of depression, anxiety, and attention problems; and (c) the global impairment scale-measures occupational, social relationships, and self-care. The HDI-S consists of 50 items using a 5-point Likert-rating scale for each item, and can be completed in 15 minutes or less (Saunders & Wojcik, 20034).

Reliability of the HDI-S in terms of internal consistency relative to the tripartite scales was determined using Cronbach's alpha. Alpha coefficients obtained for the three scales measured by the HDI-S were as follows: morale was .88, global symptoms was .95, and global impairment scale was .92. In addition, reliabilities for HDI-S subscales

ranged from .70 to .92. “Reliability estimates support the use of the HDI-S for patient diagnostic screening” (Saunders & Wojcik, 2003, p. 237). So, the HDI-S is a psychological self-inventory that is reliable as it relates to doing diagnostic work in the clinical setting.

The dependent variables used in this study were depression, anxiety, and attention problems. Each dependent variable was measured using the HDI-S and was scored based on the criteria clinicians use in assessing the mental-health status of their patients, as determined by the authors of the instrument. The HDI-S asks patients to consider their mood over the prior 2 weeks (citation). For example, psychological distress was operationalized on the HDI-S as patients who have experienced low levels of subjective well-being or morale over the past 2weeks. Morale or well-being may be otherwise described as patient’s sense of contentment, happiness, hopefulness, or recurrent positive affect (citation). The patient used a Likert-rating scale of 1–5, with 1 being *no distress*, and 5 being the *greatest distress*. Each of the scales and/or subscales in the HDI-S measuring patient psychological distress are measured on the Likert-rating scale of 1–5. The demographics used in my study were age, gender, race, ethnic identity, educational level, and socioeconomic status.

Data Analysis Plan

The statistical software, Statistical Package for the Social Sciences Version 23, was used for the descriptive and inferential analyses that were conducted. By using descriptive statistics, sample characteristics for nominal data was analyzed with percentages and frequencies. Interval and ratio data were analyzed with means and

standard deviations. Data were screened for univariate and multivariate outliers. The examination of univariate outliers was tested by creating standardized values for each scale of interest and examining cases for values that fell above 3.29 and values that fell below -3.29 (Tabachnick & Fidell, 2014). In addition, variables were assessed for normality through the calculation of skew and kurtosis measurements. Any continuous variable with a skew with magnitude greater than 2 or a kurtosis with a magnitude greater than 7 may exhibit nonnormal distributions (Kline, 2011). These were assessed with a Kolmogorov Smirnov test prior to use in the analysis. As stated previously, the primary research question addressed in this study was, Do middle-aged men who receive maintenance levels of TRT (i.e., TRT for no less than 1 year) experience a difference in levels depression, anxiety, and/or attention problems than do middle-aged men who do not receive TRT?

$H_0$1: There was no difference in the level of depression experienced by middle-aged men who are receiving maintenance levels of TRT versus men who are not receiving TRT, as measured by the HDI–S.

$H_1$2: There was a difference in the level of depression experienced by middle-aged men who are receiving maintenance levels of TRT versus men who are not receiving TRT, as measured by the HDI–S.

$H_0$2: There was no difference in anxiety experienced by middle-aged men who are receiving maintenance levels of TRT versus men who are not receiving TRT, as measured by the HDI–S.

$H_1$2: There was a difference in the level of anxiety experienced by middle-aged men who are receiving maintenance levels of TRT versus men who were not receiving TRT, as measured by the HDI–S.

$H_0$3*:* There was no difference in attention problems experienced by middle-aged men who are receiving maintenance levels of TRT versus men who are not receiving TRT, as measured by the HDI–S.

$H_1$3: There was a difference in attention problems experienced by middle-aged men who are receiving maintenance levels of TRT versus men who were not receiving TRT, as measured by the HDI–S.

To assess this study's research question and hypotheses, a MANOVA was. The MANOVA creates a linear combination of the dependent variables for a grand mean used to assess whether there are group differences between the set of dependent variables. The dependent variables; depression, anxiety, and attention problems must be continuous. Differences on the set of variables are assessed for two discreet groups (independent variables; i.e., Group A–middle-aged men who were receiving maintenance levels of TRT, and Group B–men who were not receiving TRT).

Prior to analysis, the assumptions of normality and homoscedasticity of variance/covariance matrices were assessed. Normality assumes that the scores are normally distributed (bell shaped) and was assessed using the Kolmogorov Smirnov test. According to Stevens (2016), MANOVA is robust toward violations of this assumption with respect to Type I error. Homoscedasticity of variance assumes that both groups have equal error variances and was assessed using Levene's test (Stevens, 2016).

Homoscedasticity of covariance matrices is the multivariate equivalent to homogeneity of variance and was tested using Box's *M* test (Morgan, Leech, Gloeckner, & Barrett, 2012). If the MANOVA results are statistically significant, univariate analyses of variance (ANOVAs) associated with the analysis are interpreted (Tabachnick & Fidell, 2014).

As a post hoc analysis, univariate ANOVAs are necessary if the MANOVA detects overall significance, as they identify the specific dependent variables that differ significantly between groups (Stevens, 2016). As such, a significant finding on the MANOVA led the researcher to conduct one ANOVA on each dependent variable (see Stevens, 2016). For any of these univariate ANOVAs that indicated significant differences on a specific dependent variable, Tukey's post-hoc analysis was conducted to determine which groups differ from the others (see Stevens, 2016). These analyses determine whether each group has significantly higher or lower scores than each other group through a series of pairwise comparisons. In these comparisons, each of the potential pairs of groups are tested for significant differences (Stevens, 2016). This is the final stage in the MANOVA and indicates which of the groups (based on the categorical independent variable) have the highest and lowest scores on any significant dependent variable (Stevens, 2016).

Threats to Validity

There were two potential threats to internal validity. The first threat to internal validity was environmental variables. The research participants were drawn from four different doctors' offices. The doctors' offices were in suburban communities in northeastern Ohio. The data were collected during normal business hours. The second

threat to internal validity was assignment bias. The patient populations were demographically similar, as were the office facilities, and conditions.

There were no significant threats to external validity, as the researcher reported the findings of the present study objectively, regardless of his personal beliefs or desires. Also, there were no artifacts that would influence or distort measurements.

Ethical Procedures

Permission to conduct this study was ascertained from the Committee on Ethical Standards in Research for the IRB at Walden University prior to the initiation of this research study. The Walden IRB approval number is 04-19-18-0079448. Permission was ascertained from a primary-care physician, and three physicians who specialize in hormone-replacement therapy to have patients from their practices participate in this study.

If the research participant wished to receive information about the results of the study he would be able to ascertain a copy of study results at his physician's office after study completion. Research participants were informed that completing the research survey should take no longer then 10 to 15 minutes, and that all data collected were anonymous. There was minimal risk associated with participation in this study.

Summary

This study sought to determine if there are differences in depression, anxiety, and/or attention problems experienced by middle-aged men who receive maintenance levels of TRT versus men who have not receive TRT. In Chapter 4, I will report the research findings of this study.

Chapter 4: Results

Introduction

The purpose of this study was to discover if there were any clinically significant differences in the levels of depression, anxiety, or problems with attention experienced by middle-aged men who receive maintenance-level doses of TRT (i.e., receiving TRT for at least 12 months) versus middle-aged men who do not receive TRT. Research hypotheses for this research study, in brief, were

$H_0$1: There was no difference in the level of depression, anxiety, and/or attention issues experienced by middle-aged men who were receiving maintenance levels of TRT versus men who were not receiving TRT.

$H_1$1: There was a difference in the level of depression, anxiety, and/or attention issues experienced by middle-aged men who were receiving maintenance levels of TRT versus men who were not receiving TRT.

This chapter reports on data-collection procedures as compared to the plan presented in Chapter 3. Also reported here were the results of the data collected from research participants.

Data Collection

The time frame for data collection was June through October 2018. Response rates were very good. There were 198 individuals invited to participate in my study. Of the 198 individuals invited to participate, self-report inventories were collected from 179 total research participants. The sample was comprised of middle-aged men (ages 45–64). The sample for this study was a nonprobability sampling; specifically, it was a sample of

convenience. The sample was comprised of middle-aged White and African American men. It was proportional to the larger population of White and African American men.

Tables 1 and 2 display sample characteristics for the nominal and continuous variables collected, respectively.

Table 1

Frequency Table for Nominal Variables

Testosterone replacement therapy (TRT) variable	*n*	%
No TRT	89	49.72
TRT	90	50.28
Missing	0	0.00

The average depression score was 50.22 (*SD* = 11.32, *SEM* = 0.85, minimum [min] = 15.00, maximum [max] = 85.00). The average anxiety score was 51.42 (*SD* = 10.26, *SEM* = 0.77, min = 40.00, max = 85.00). The average attention score was 51.07 (*SD* = 9.87, *SEM* = 0.74, min = 41.00, max = 85.00). Also, skewness and kurtosis were calculated and are shown in Table 2. When the skewness is greater than 2 in absolute value, the variable is considered to be asymmetrical about its mean (Westfall & Henning, 2013). When the kurtosis is greater than or equal to 3, then the variable's distribution is markedly different than a normal distribution in its tendency to produce outliers (Westfall & Henning, 2013). The skewness and kurtosis values suggest that the variables are normally distributed.

Table 2

Summary Statistics Table for Interval and Ratio Variables

Variable	*M*	*SD*	*n*	*SEM*	Skewness	Kurtosis
Depression score	50.22	11.32	179	0.85	0.88	0.70
Anxiety score	51.42	10.26	179	0.77	1.06	0.48
Attention score	51.07	9.87	179	0.74	0.79	0.06

Results

A MANOVA was conducted to assess if there were significant differences in the depression scores, anxiety scores, and attention scores between men who were receiving TRT versus men who were not receiving TRT. Prior to the analysis, univariate outliers were examined for the dependent variables. An outlier was defined as any value that falls outside the range of +/- 3.29 standard deviations from the mean (Tabachnick & Fidell, 2013). The attention score had one outlier. This outlier was examined, and it was determined that the outlier was not due to a data entry error. Further, the analysis was conducted with this outlier removed to determine its impact on the results. The results of the analysis did not change after removing the outlier. Therefore, this case was not excluded from the final reported analysis.

The assumptions of independence of observations, normality, and homoscedasticity were assessed. Each observation in the data came from a unique participant, so the independence of observations was met. To assess the assumption of multivariate normality, Mahalanobis distances were calculated for the residuals and

plotted against the quantiles of a chi-square distribution (see DeCarlo, 1997; Field, 2013). Normality can be assumed if the points form a relatively straight line. The scatterplot for normality is presented in Figure 1. The points deviate from the normal line; however, the skewness and kurtosis values for the dependent variables suggested that the data were normally distributed, and according to Stevens (2016), MANOVA is robust toward violations of this assumption with respect to Type I error. Therefore, the analysis was continued.

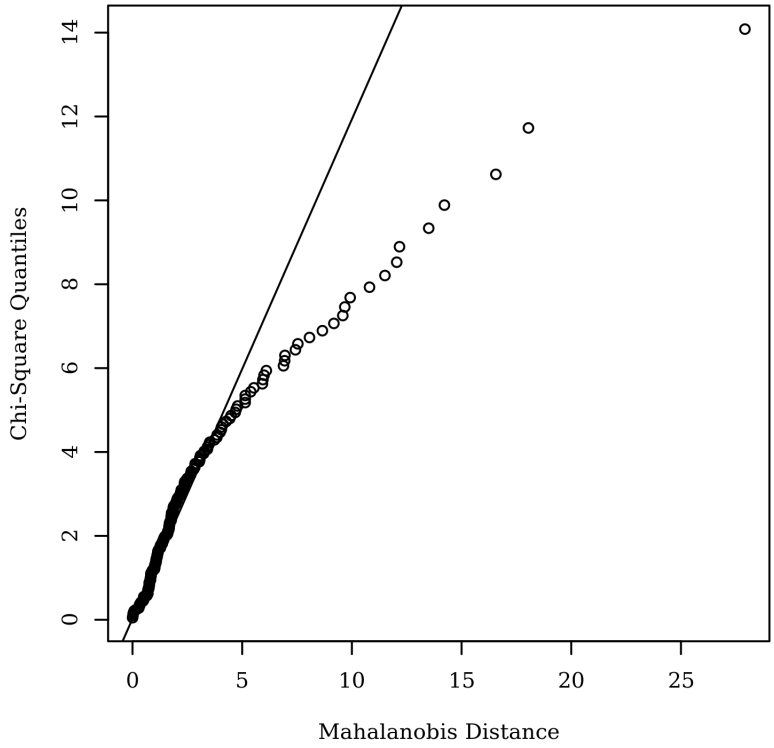

Figure 1. Mahalanobis distance scatterplot testing multivariate normality.

To examine the assumption of homoscedasticity, Box's *M* test was conducted. The results were not significant at the .001 level, $\chi^2(6) = 17.82$, $p = .007$, indicating that the

covariance matrices for each group of TRT were not significantly different from one another and that the assumption was met.

The results of the MANOVA appear in Table 3. The main effect for TRT was significant, $F(3, 175) = 3.25$, $p = .023$, $\eta^2 p = 0.05$, suggesting that depression score, anxiety score, and attention score were significantly different between the levels of TRT. To further examine the effects of TRT on depression score, anxiety score, and attention score, an ANOVA was conducted for each dependent variable.

Table 3

Multivariate Analysis of Variance Results for Depression, Anxiety, and Attention by Testosterone Replacement Therapy (TRT)

Variable	Pillai	*F*	*df*	Residual *df*	*p*	η_p^2
TRT	0.05	3.25	3	175	.023	0.05

The results of the ANOVA for depression score were significant, $F(1, 177) = 5.36$, $p = .022$, indicating there were significant differences in depression score among the levels of TRT (Table 4). Depression scores indicate that there was a statistically significant difference between Group A (nontreatment group) and Group B (treatment group). Group B had lower depression scores than Group A. So, the null hypothesis was rejected. The eta squared was 0.03, indicating TRT explains approximately 3% of the variance in depression score. Cohen's *d* was 0.35, indicating a small effect size (see Cohen, 1988). The means and standard deviations are presented in Table 5 and displayed visually in Figure 2.

Table 4

Analysis of Variance Table for Depression Score by Testosterone Replacement Therapy (TRT)

Term	*SS*	*df*	*F*	*p*	η_p^2
TRT	669.69	1	5.36	.022	0.03
Residuals	22125.37	177			

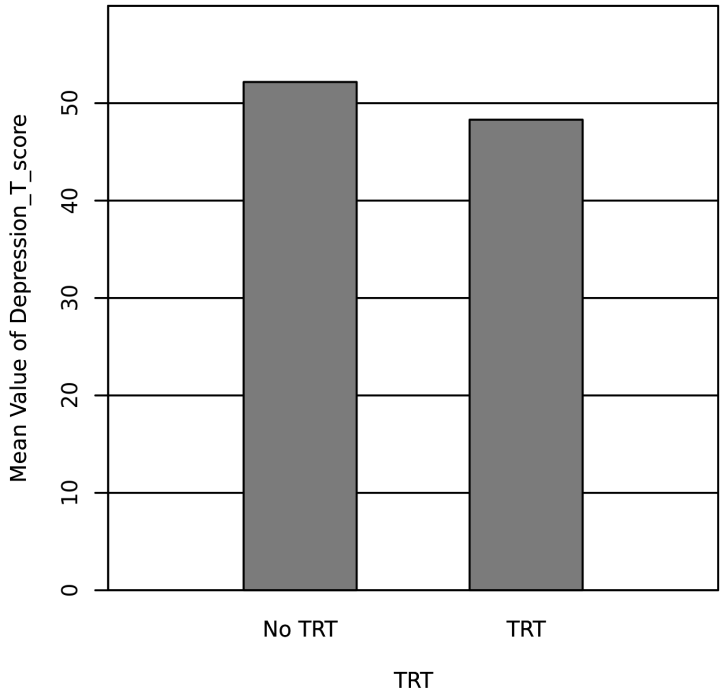

Figure 2. Depression score means by factors levels of testosterone replacement therapy (TRT).

Table 5

Mean, Standard Deviation, and Sample Size for Depression Score by Testosterone Replacement Therapy (TRT)

Combination	*M*	*SD*	*n*
No TRT	52.17	11.72	89
TRT	48.30	10.62	90

The results of the ANOVA for anxiety score were significant, $F(1, 177) = 4.00$, $p = .047$, indicating there were significant differences in anxiety score among the levels of TRT (Table 6). The eta squared was 0.02 indicating TRT explains approximately 2% of the variance in anxiety score. Cohen's *d* was 0.30, indicating a small effect size (see Cohen, 1988). Anxiety scores indicate that there was a statistically significant difference between Group A (nontreatment group) and Group B (treatment group). Group B had lower anxiety scores than Group A. So, the null hypothesis was rejected. The means and standard deviations are presented in Table 7 and displayed visually in Figure 3.

Table 6

Analysis of Variance Table for Anxiety Score by Testosterone Replacement Therapy (TRT)

Term	*SS*	*df*	*F*	*p*	η_p^2
TRT	414.62	1	4.00	.047	0.02
Residuals	18329.11	177			

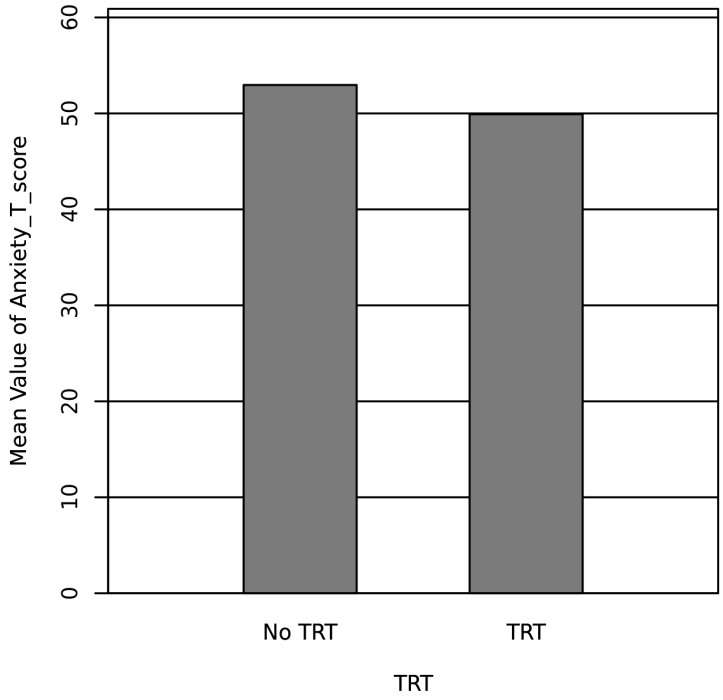

Figure 3. Anxiety score means by factors levels of testosterone replacement therapy (TRT).

Table 7

Mean, Standard Deviation, and Sample Size for Anxiety Score by Testosterone Replacement Therapy (TRT)

Combination	*M*	*SD*	*n*
No TRT	52.96	10.67	89
TRT	49.91	9.66	90

The results of the ANOVA for attention score were significant, $F(1, 177) = 9.58$, $p = .002$, indicating there were significant differences in attention score among the levels

of TRT (Table 8). The eta squared was 0.05 indicating TRT explains approximately 5% of the variance in attention score. Cohen's *d* was 0.46, indicating a small effect size (see Cohen, 1988). Attention scores indicate that there was a statistically significant difference between Group A (nontreatment group) and Group B (treatment group). Group B had lower attention scores than Group A. So, the null hypothesis was rejected. The means and standard deviations are presented in Table 9 and displayed visually in Figure 4.

Table 8

Analysis of Variance Table for Attention Score by Testosterone Replacement Therapy (TRT)

Term	*SS*	*df*	*F*	*p*	η_p^2
TRT	889.74	1	9.58	.002	0.05
Residuals	16442.31	177			

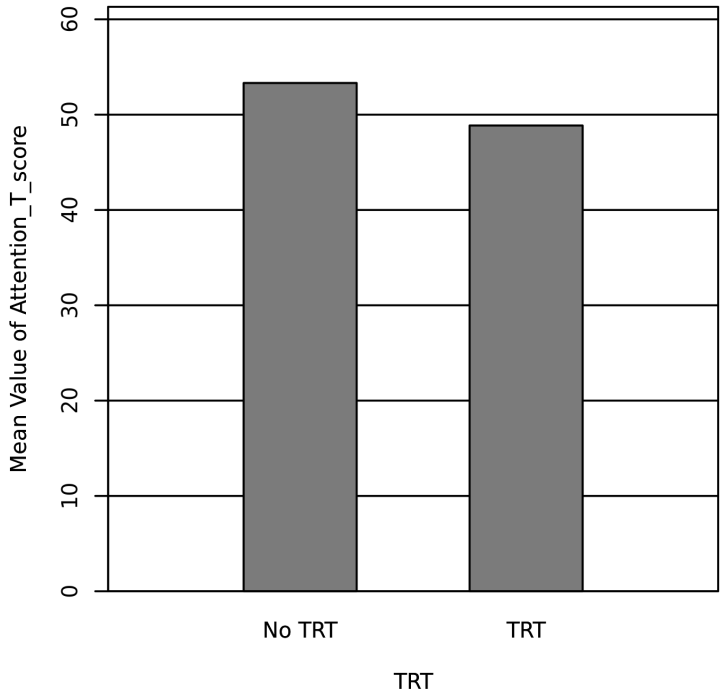

Figure 4. Attention score means by factors levels of testosterone replacement therapy (TRT).

Table 9

Mean, Standard Deviation, and Sample Size for Attention Score by Testosterone Replacement Therapy (TRT)

Combination	*M*	*SD*	*n*
No TRT	53.31	10.54	89
TRT	48.86	8.65	90

Summary

The research question addressed in this study was, Do middle-aged men who receive maintenance levels of TRT (i.e., TRT for no less than 1 year) experience a difference in levels of depression, anxiety, or attention problems than do middle-aged men who do not receive TRT?

This research study found that there was a statistically significant difference, although a small size effect, in the level of depression, anxiety, and/or attention issues experienced by middle-aged men who are receiving maintenance levels of TRT versus men who are not receiving TRT. The middle-aged men who had been receiving TRT for 12 months or longer had lower levels of depression, anxiety, and attention issues. So, the null was rejected.

In Chapter 5, I will provide an interpretation of my study's findings, discuss limitations of the study, make recommendations for further study, discuss the implications of my study, and conclude with a brief statement about the essence of my study.

Chapter 5: Discussion, Conclusions, and Recommendations

Introduction

The purpose of this study was to determine if there were clinically significant differences in levels of depression, anxiety, or attention issues experienced by middle-aged men who received TRT verses middle-aged men who did not. In doing the literature review for this study, I unearthed no research on this topic previously conducted by psychology researchers. Since depression, anxiety, and attention problems are the domain of psychologists, this study was conducted to gain insight on this topic from the perspective psychologists bring to research. The problem addressed by this study was that as men move through the life span, many begin to experience or have an increased experience of mental health issues such as depression, anxiety, and attention problems (Charlton, 2004). Also, there had been very little medical research about the psychological symptoms middle-aged men may experience as they move through the life span related to a decrease in testosterone levels (P. B Gray et al., 2005; Hintikka et al., 2009; Moffat et al., 2002; Rizvi et al., 2010; Wang et al., 2004; Wang et al., 2000; Wu et al., 2010).

Of greater significance in relation to this study was that scholars in clinical psychology have done very little, if any, research on the psychological impact of TRT in middle-aged men who experience depression, anxiety, and/or attention problems (P. B Gray et al., 2005; Hintikka et al., 2009; Moffat et al., 2002; Rizvi et al., 2010; Wang et al., 2004; Wang et al., 2000; Wu et al., 2010).

This was a quantitative study that used a psychological self-report inventory designed to assess the psychological state of mind of respondents. The survey instrument used in this study was a psychological self-report inventory that measures the key variables of concern: depression, anxiety, and/or attention problems. The independent variable was the use of TRT at maintenance levels for at least 12 months. The dependent variables were depression, anxiety, and attention problems. The resulting data were analyzed using the MANOVA.

This study found that middle-age men who were recipients of TRT demonstrated statistically significant lower levels of depression, anxiety, and/or attention issues. However, when Cohen's *d* was applied to each of this study's dependent variables, only a small size effect was found. Depression had a Cohen's $d = .35$, anxiety had a Cohen's $d = .30$, and attention had a Cohen's $d = .46$. Each of the post hoc analyses indicate a small clinical significance for each of the dependent variables. These findings suggest that if TRT is to be used by a physician to help in reducing a middle-aged male patient's level of depression, the physician should complete a thorough risk/benefit analysis with the patient. A risk/benefit analysis would give the patient enough data to determine if TRT is the best possible choice for him.

Interpretation of the Findings

As seen in Chapter 2, some medical researchers believe that TRT can have a mitigating effect on depression while others disagree (see Wu et al., 2010). The scholarly research available focuses on the relationship of testosterone levels in men to men's experience of depression, although some of the same literature makes mention of

testosterone levels being related to other mental-health issues faced by men as they move along the life span (Khera et al., 2012). Such issues included, but were not limited to, depression, anxiety, sleep disturbance, and/or attention problems (Khera et al., 2012). The relationship between decreasing levels of testosterone in men as they age, hypogonadism, and LOH has been, and continues to be, the subject of some debate and controversy (Emmelot-Vonk et al., 2008), although the most current literature seems far less the subject of debate or controversy, as the positive effects of TRT on mood in men appear to have become more accepted. Emmelot-Vonk et al. (2008) postulated that the mixed findings in previous studies are likely due to differences in study designs, including such things as the age of research participants, gonadal status, research participant general health status, method of treatment administration, duration of treatment, instrumentation used to study aging, and/or laboratory methods used to assess testosterone levels in male research participants.

The scholarly research available focused on the relationship of testosterone levels in men to men's experience of depression, although some of the same literature makes mention of testosterone levels being related to other mental health issues faced by men as they move along the life span. Such issues included, but were not limited to, depression, anxiety, sleep disturbance, and/or attention problems (Khera et al., 2012). For the purpose of this study, the dependent variables selected included depression, anxiety, and attention problems. Insomnia was not selected for this study. That said, insomnia is a potential dependent variable for future study.

The results of this study confirm the findings of medical researchers who have found that TRT has a mitigating effect on depression in middle age men (P. B Gray et al., 2005; Hintikka et al., 2009; Moffat et al., 2002; Rizvi et al., 2010; Wang et al., 2004; Wang et al., 2000; Wu et al., 2010). The medical researchers who have found a mitigating effect on depression make note that among the symptoms of depression they found irritability (citation). However, irritability can be a feature of anxiety disorders (American Psychiatric Association, 2013). These medical researchers did not look at anxiety as an issue in their research studies (see P. B Gray et al., 2005; Hintikka et al., 2009; Moffat et al., 2002; Rizvi et al., 2010; Wang et al., 2004; Wang et al., 2000; Wu et al., 2010).

Many middle-aged men, and men in late life, complain of reduced mental clarity, acuity, and ability to focus (Emmelot-Vonk, 2008). This study extends the knowledge in the discipline of psychology by tending to confirm what some medical researchers have found regarding TRT and its mitigating effect on depression, as well as the impact of TRT on anxiety and attention issues which had not been previously studied. What this study found was that there was a statistically significant difference between research participant groups, but post hoc analysis found a small clinically significant beneficial effect on middle age men who received TRT versus men who did not.

Limitations of the Study

This research project had a sample size of 179 middle age men, is sufficient to reject a false null hypothesis. The power calculator G*Power was used to conduct the power analysis to determine the sample size for this study found that adequate power

would be obtained with a total of 180 research participants, with 90 research participants in each of the two study groups (see Faul et al., 2008). Research participants were White American and Black American men. The research participants that comprised the sample for this study were limited insofar as cultural orientation is concerned. The population of the United States is much more culturally diverse than the sample of research participants who participated in this study. The sample of research participants in this study was not reflective of the great diversity of cultures represented in the social context of the United States.

The sampling method used in this study was a nonprobability sampling method. Specifically, the method used in this study was convenience sampling (Gravetter & Forzano, 2012). According to Gravetter and Forzano (2012), convenience sampling is a method of sampling that is often used in behavioral science research simply because research participants are easy to get. Convenience sampling is considered to be a weak form of sampling (Gravetter & Forzano, 2012). This form of sampling is not randomized, and the researcher makes no attempt to know the population as was the case in this study (Gravetter & Forzano, 2012). However, in this study I identified research participants by age and gender. Because of the lack of randomness in convenience sampling and consequently in this study, there was a possibility that the sample could have been biased (see Gravetter & Forzano, 2012). The sample came from four doctors' offices and the participants may have participated in this study because of strong feelings they may have heard expressed in those settings as to the benefit of TRT.

I used a quasi-experimental research strategy, which constitutes a limitation. The quasi-experimental research strategy has some of the rigor of an experimental research strategy, but it has a flaw (Gravetter & Forzano, 2012). The flaw is that, unlike experimental research strategy, the quasi-experimental research strategy precludes ascertaining a cause and effect (i.e., causation) answer to the research question (Gravetter & Forzano, 2012). However, using the quasi-experimental design, I was to determine if there is a correlation/relationship between the independent and dependent variables that have been assessed for each research participant (see Gravetter & Forzano, 2012). I found that there is a correlation between the study's independent and dependent variables.

The use of a self-report psychometric instrument gives a glimpse as to whether TRT had a psychological impact on middle-aged men. In addition, self-report inventories are inherently subjective, so inaccurate responses may not have been entirely avoided (Gravetter & Forzano, 2012). Also, in the control group (Group B) it is possible there were men who needed TRT but never received it, and men who do not need to receive TRT because they were not hypogonadal. These data were not available for this study due to the anonymity of research participants.

According to Emmelot-Vonk et al. (2008), differences in research study findings may be due to differences in such things as the method of administration of TRT used to treat hypogonadal men because the level of efficacy among the methods of administration may vary significantly. Examples of such methods include oral or intramuscular TUs, topical gels, and a roll-on application applied to the underarms (Emmelot-Vonk et al., 2008). These are examples of different formulations and methods of administration of

TRT to each patient that could impact the size effect found for each dependent variable (Emmelot-Vonk et al., 2008).

This study confirms the findings of prior research studies, such as Wang et al.(2004) and Wang et al. (2000), which demonstrated a clinically significant reduction in symptoms of depression in middle-aged men. Nonetheless, the findings of my study should be read with some caution, as there were data about each of the research participants that was unknown to the researcher.

Lack of funding was a limiting factor for conducting this study. Also, the populations from which research participants were recruited were self-selecting. Physicians could be a source of bias for research studies of this type. Some physicians believe that TRT is preferred treatment for men in middle age and older. On the other hand, there are physicians who do not see the value in TRT. Physicians who regularly prescribe HRT for men and women will have a favorable bias toward TRT. On the other hand, physicians who do not use HRT for their male and female patients who might benefit from it may demonstrate a negative bias. Such bias could impact study results as the bias of a patients may be reflective of their physician's view.

Recommendations

This study has highlighted that there has been a dearth of research studies conducted by psychology researchers as it pertains to the relationship between Hypogonadism and both the negative and positive dimensions of mood in middle-aged men. Based on a review of the current literature, there has been no research study that has looked beyond the impact of TRT on depression to include anxiety and/or attention. This

study only begins to explore the range of research studies psychologists might conduct on middle-aged hypogonadal men.

Some possible studies research psychologists might conduct include, but are not limited to, additional studies focusing on the impact of TRT on depression, anxiety, and attention, as well as insomnia, which has not yet been studied. Studies should examine the impact of TRT on energy level, fatigue, and lethargy, as well as the ability to engage in vigorous physical activity. Also, studies could include three research participant groups: one group of hypogonadal middle-aged men who have received TRT for 12 months or longer, a second group of middle-aged men who have hypogonadal status but who are not receiving TRT, and a third group of middle age men who are not hypogonadal and do not receive TRT. Ideally this study would be completed using an experimental design.

Other studies might include the impact of TRT on neurocognitive function using neuropsychological test batteries, the impact of TRT on neurocognitive decline in middle-aged men, the impact of TRT on mental acuity, and the impact of TRT on memory. Also, studies that include visuospatial cognition, visual memory (immediate and delayed), as well as the impact of TRT on increasing the positive aspects of mood in hypogonadal middle age men.

Additionally, research psychologists might examine the qualitative impact of decreased negative aspects of mood and/or increased positive aspects of mood on spouses or significant others of hypogonadal middle-aged men who receive TRT as opposed middle-aged men who did not.

Implications

The potential impact for positive social change from this study was first to contribute to the scientific knowledge base in the field of psychology by its investigation of the relationship between TRT and mental-health issues among middle-aged men. On the individual level, gaining an understanding the impact of TRT in this population as it relates to mental-health issues among middle-aged men may increase clinician capacity to reduce the negative impact mental-health issues can have in this population and consequently increase the patient's positive experience of his own quality of life.

It should be noted here that over the past 75 year the life span of both men and women have dramatically increased (Crimmins, 2015). Prior to the last century there were very few countries that had life expectancy that surpassed 50 years of age (Crimmins, 2015). According to Crimmins (2015), the life expectancy of women and men has risen from age 65 to age 85 by approximately 50% over the last 75 years (Bell & Miller, 2005). As the human life span has increased, so too has the incidence of obesity, diabetes and MetS (Crimmins, 2015). According to Giltay et al. (2010), obesity, diabetes, and MetS are comorbid with hypogonadism, which negatively impacts depression symptoms in middle-aged men. Also, according to Skilton, Moulin, Terra, & Bonnet (2007), metabolic issues and their comorbidity with hypogonadism tend to negatively impact both depression and anxiety.

It should be noted that the dramatic increase in the human life span over the past 50 to 75 years has not allowed for the development of studies by psychologists that examine the relationship between mood and hypogonadism. Fifty- to 75-years ago the

human life span was only 50-55 years of age (Crimmins, 2015). So, it has been a relatively short period of time during which such research could have been conducted by researchers in the field of psychology.

This study has confirmed a beneficial impact of TRT in middle-aged men. While the size effect was small, it was positive. As found in the literature review conducted for this study, as men age there is an inverse correlational with their level of BT. As men age, the BT level will diminish. Medical research has not demonstrated any horrible side effects resulting from testosterone supplementation as have many medications that are routinely prescribed to patients with diseases such as cancer. On the other hand, according to the American Dental Association (2018), the addition of fluoride to the drinking water supply in the United States for the past 70 years has resulted in a 25% decrease in cavities and tooth decay for citizens. Some would argue that 25% is a small size effect, but it cannot be argued that the beneficial impact does not enhance quality of life of people and should therefore be discontinued. Given what we know about hypogonadism and the beneficial effect of testosterone supplementation on mood, TRT could someday be used to promote good mental health much in the same way fluoride is used to promote good dental health.

On an organizational level, this study may advance mental-health practice. Current medical practice routinely includes examination of medical issues that can effect mood, such as thyroid issues, MetS, obesity, and diabetes. The advance in mental health would be the addition of testing to determine if a middle-aged male patient experiencing

depression, anxiety, and/or attention problems, is a candidate for TRT to aid in addressing his emotional distress.

On a societal level, I hope that other scholar practitioners in the field of psychology may be inspired to extend this research topic area. If enough empirical data becomes available through research psychologists, then what would be necessary to create public health policy that embraces, or dissuades, the use of TRT in middle-aged men who are experiencing the negative effects of hypogonadism.

This study may provide some guidance to medical clinicians, such as psychiatrists, primary-care physicians, and endocrinologists, as well as clinical psychologists who see middle-aged men in their practice settings. This provides another avenue that may serve to connect medical practitioners with clinical psychologists so that their mutual patients may gain the greatest possible benefit from their discreet areas of health care practice, as they complement each other.

Conclusion

Men who have reached middle-age may think that not feeling as good as they did when they were younger is just a fact of life related to movement through the life span. There is no question that men do experience some decline over the course of time. However, depression, anxiety, and/or attention related concerns are not necessarily just a fact of age. There are physiological issues such as hypogonadism, which can be exacerbated by or be comorbid with conditions like diabetes, obesity, and MetS. These men may benefit from TRT, but further research would be required to determine whether this is the case.

This study has shown that, statistically speaking, middle-aged men who receive TRT experience less depression, anxiety, and attention issues, although the size effect was small. Further research is needed to definitively determine the extent of size effect of TRT among middle-aged men.

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