Exercise dosages for the management of generalized anxiety disorder: A scoping review

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DECLARATION

I, Natalie Leander, declare that this Research Report is my own, unaided work. It is being submitted for the Degree of Master of Science in Physiotherapy at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any other University.

_____ (Signature of candidate)

31th day of May 2024 in Randburg.

DEDICATION

I dedicate this research report to my husband, without whom none of this would be possible and my son, my reason to do better and be better. And lastly, as a thanks to my parents for all they have done and continue to do for our family.

ABSTRACT

Objective: This review was conducted to map the extent of evidence relating to the dosage of exercise for anxiolytic effect, in youth and adolescents with Generalized Anxiety Disorder (GAD).

Introduction: Exercise is known for its benefit to people living with depression and anxiety in adult populations. Less is known about the differences in exercise prescriptions used for the management of anxiety subtypes in younger populations. The rationale for this topic in adolescents and youths, living with GAD was to ascertain the extent to which this cohort has been studied regarding the use of exercise in the treatment of anxiety and which dosages were used.

Inclusion criteria: All studies with participants aged 10-24 years of age with a GAD diagnosis, were considered, where exercise was used as part of the management of their anxiety. No restrictions were placed on study types.

A scoping review was performed using the JBI methodology. Databases searched included Pubmed, PEDro, Cochrane database of systematic reviews and Cinahl Ultimate along with grey literature databases. No time restrictions were applied, and all types of research articles were considered. The charted data was tabulated using a modified JBI data extraction instrument.

The initial result of 728 results was reduced to four studies that met with inclusion criteria. The final four studies had populations in the upper range of between 18 to 24 only. No applicable data was found in the 10 to 17-year age range. The exercise types used in these four studies were treadmill running, Pilates, lower limb strengthening and dynamic cycling. Two studies incorporated a single bout of vigorous treadmill running for 30 minutes. One study did a single bout of beginner Pilates for 30 minutes and the last study used lower limb strengthening and dynamic cycling biweekly for six weeks.

The literature on exercise dosage for the management of GAD in adolescents and youth is severely limited. Data on exercise for specific subtypes of anxiety in adolescents and youth seems to be limited in general as well. This is an important area for research as anxiety starts in early childhood and GAD in particular has a peak age of onset of 15 years. It seems feasible to try and approach anxiety in youth and adolescents with non-invasive therapies such as exercise but there is a definite gap in the literature regarding its use in managing GAD.

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NOMENCLATURE

AACAP: American Association of Child and Adolescent Psychiatry

A professional association facilitating child and adolescent psychiatric care.

ACTH: Adrenocorticotropic hormone

A tropic hormone produced in anterior pituitary, involved in cortisol regulation (Allen and Sharma, 2023).

ADHD: Attention deficit hyperactivity disorder

A neurodevelopmental disorder characterized by inattention, hyperactivity and/or impulsivity (Hopkinsmedicine.org, 2024).

AGAD: Analogue generalized anxiety disorder

Subclinical or subsyndromal GAD is referred to as Analogue Generalised Anxiety Disorder (AGAD) (Volz et al., 2022).

AVP: Arginine Vasopressin

A hormone synthesized in the hypothalamus, known for involvement with blood pressure regulation, osmotic balance and kidney function (Cuzzo et al., 2024)

BDNF: Brain-derived neurotrophic factor

BLA: Basolateral amygdala

“a temporal lobe structure that contributes to a host of behaviours.” (Polepalli et al., 2020)

BNST: Bed nucleus of the stria terminalis

“The bed nucleus of the stria terminalis (BNST) is a centre of integration for limbic information and valence monitoring.” (Lebow and Chen, 2016)

CBT: Cognitive behavioural therapy

It is a method of psychotherapy that aims to address specific unhelpful thought processes, beliefs and behaviours. Through this method, the patient comes to understand their disorder and is taught coping skills such as relaxation techniques to help with the management of the anxiety (Wolgensinger, 2015).

CFR: Corticotroph-releasing hormone

“Corticotropin-releasing hormone is the central regulator of the hypothalamic-pituitary-adrenal (HPA) axis, which is the main organizer of the body’s response to stress.” (Slominski, 2009)

DSM-IV: Diagnostic and statistical manual of mental disorders

fMRI: Functional magnetic resonance imaging

“a class of imaging methods developed in order to demonstrate regional, time-varying changes in brain metabolism.” (Glover 2011).

GAD: Generalised anxiety disorder

A psychological condition broadly characterised by continuous, excessive anxiety and worry for longer than six months (Stein and Sareen, 2015).

HIIT: High-intensity interval training

“episodic short bouts of high intensity exercise separated by short periods of recovery at a lower intensity.” (Campbell et al., 2019)

HPA: Hypothalamic-Pituitary-Adrenal Axis

The HPA-axis neuroendocrine system controls glucocorticoid hormone production and secretion (Spencer and Deak, 2017).

MeSH: Medical subject headings

“The Medical Subject Headings (MeSH) thesaurus is a controlled and hierarchically-organized vocabulary produced by the National Library of Medicine. It is used for indexing, cataloguing, and searching of biomedical and health-related information” (National Library of Medicine, 2024)

NPI: Non-pharmacological interventions

“Non-pharmacological interventions (NPI) are any non-chemical intervention (theoretically supported) performed on and benefitting the patient” (Physiopaedia.com)

OCD: Obsessive-compulsive disorder

“Recurrent and persistent thoughts, urges or images that are experienced, at some time during the disturbance, as intrusive, unwanted, and that in most individuals cause marked anxiety or distress.” (DSM-5)

ODD: Oppositional defiant disorder

“Oppositional defiant disorder (ODD) is a type of childhood disruptive behaviour disorder that primarily involves problems with the self-control of emotions and behaviours” (Aggarwal et al., 2022)

PD: Panic disorder

“an anxiety disorder characterized by recurrent, unexpected panic attacks that are associated with (a) persistent concern about having another attack, (b) worry about the possible consequences of the attacks, (c) significant change in behaviour related to the attacks (e.g., avoiding situations, engaging in safety behaviour, not going out alone), or (d) a combination of any or all of these.”(DSM -5-TR)

PSWQ: Penn State Worry Questionnaire

The PSWQ is a 16-item self-report scale designed to measure the trait of worry in adults. (Meyer et al., 1990)

PTSD: Post-traumatic stress disorder

“Posttraumatic stress disorder (PTSD) is a prevalent and complex psychiatric condition that arises in response to exposure to traumatic events, significantly impacting an individual's mental well-being.” (Mann et al., 2024)

SAD: Separation anxiety disorder

“Developmentally inappropriate and excessive anxiety concerning separation from home or from those to whom the individual is attached” (DSM-5-TR).

SNRI: Serotonin-norepinephrine reuptake inhibitors

A class of medication used to inhibit the reuptake of serotonin and norepinephrine thereby increasing thereby activity (Sansone et al., 2014)

sAA: Salivatory alpha-amylase

An enzyme found in the oral cavity.

SSRI: Selective serotonin reuptake inhibitors

A class of medication aimed at inhibiting the serotonin transporter and inhibiting serotonin reuptake and thereby increasing its activity (Chu et al., 2024).

WHO: World Health Organisation

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CHAPTER ONE:

1.1 Introduction

Anxiety is a response to perceived danger or threatening stimuli that should result in defensive behaviours to prevent or reduce harm (Babaev et al., 2018). Generalized anxiety disorder (GAD) is a psychological condition broadly characterised by continuous, excessive anxiety and worry for longer than six months (Stein and Sareen, 2015). Generalized anxiety disorder differs from normative anxiety in that the response to danger or threatening stimuli is incessant and disproportionate (Beesdo et al., 2009). Results from the Global Burden of Disease Study, 2019, indicated that anxiety disorders steadily increase annually and that the number of anxiety disorders increased by 50% from 1990 to 2019 (Yang et al., 2019).

Masi et al. (2004) reported that 56% of children and adolescents with GAD have depression as a comorbidity. A large study conducted on Iranian youths aged six to 18 years indicated that the other most common co-existing conditions of GAD in descending order are, separation anxiety disorder (SAD), oppositional defiant disorder (ODD), social phobia, agoraphobia, attention deficit hyperactivity disorder (ADHD), obsessive-compulsive disorder (OCD), elimination disorders (enuresis and encopresis) and eating disorders (Mohammadi et al., 2020). This study also found that the prevalence of mood disorders comorbid with GAD, like depression, increased with age in contrast with elimination disorders that decrease with maturation.

The prevalence of GAD is more common in females and is often related to chronic environmental stress (Craske and Stein, 2016). Pavlova et al. (2022) looked at families and the relationship between parental anxiety and the likelihood of their children developing anxiety disorders. They found that the lifetime prevalence of anxiety in children increased proportionately to whether their parents had no anxiety disorders, one parent presented with an anxiety disorder or both parents suffered from anxiety disorders.

Generally, initial treatment for GAD is usually pharmacological. The most common medications include selective serotonin reuptake inhibitors (SSRI) or serotonin-norepinephrine reuptake inhibitors (SNRI). In children and youth, psychoeducation and cognitive behavioural therapy (CBT) are the first line of treatment and for more severe cases the combination of SSRIs and CBT is recommended by the American Association of Child and Adolescent Psychiatry (AACAP) (Dillon-Naftolin, 2016). Treatment compliance with these medications may be affected by side effects, including but not limited to nausea, headaches, uneasiness, poor sleep, gastrointestinal interference and weight gain. These side effects are very similar to symptoms of GAD (Gomez et al., 2018). Compliance is also affected by withdrawal symptoms that may ensue if dosages are missed (Dillon-Naftolin, 2016).

Benzodiazepines have been shown to be effective in reducing anxiety symptoms in the short term. Their use is limited due to the risk of abuse and adverse effects including cognitive impairment, and withdrawals when medication is ceased (Locke et al., 2015). Benzodiazepines have a delayed anxiolytic effect which makes it necessary to look at non-pharmacological interventions in the management of GAD (Gale and Millichamp, 2011). Benzodiazepines are not commonly prescribed to youth and adolescents due to a lack of data and the risk of abuse (Dillon-Naftolin, 2016).

Non-pharmacological interventions (NPI) include cognitive behavioural therapy (CBT) and exercise, yoga, mindfulness and tai-chi (Saheed et al., 2019). Cognitive Behavioural Therapy is the most commonly used form of NPI and is an effective part of primary management alone or combined with medications (Locke et al., 2015). It is a method of psychotherapy that aims to address specific unhelpful thought processes, beliefs and behaviours. Through this method, the patient comes to understand their disorder and is taught coping skills such as relaxation techniques to help with the management of the anxiety (Wolgensinger, 2015).

Exercise has been shown to have a positive effect on mood disorders, including the reduction of symptoms related to anxiety and stress-related disorders (Stubbs et al., 2017). Physical exercise is defined by the World Health Organisation as “a subcategory of physical activity that is planned, structured, repetitive, and purposeful in the sense

that the improvement or maintenance of one or more components of physical fitness is the objective" (WHO, 2010). Changes in anxiety are brought about by the effect of exercise on different physiological and psychological mechanisms. They include changes to the Hypothalamic-Pituitary-Adrenal Axis (HPA), where the influence of exercise helps with the regulation of anxiety (Anderson and Shivakumar, 2013). In terms of psychology, anxiety sensitivity has also been shown to decrease with exposure to physical exercise (Anderson and Shivakumar, 2013). Exercise may have a positive effect on GAD but the research supporting exercise as a part of a treatment strategy for anxiety-related disorders is however scattered among variations of exercises for different durations and frequencies.

Exercise prescription falls within the purview of professionals such as physiotherapists that have the knowledge base to prescribe exercise for rehabilitation post injury, management and progression of fitness for lifestyle and sports related needs. Strengthening, conditioning, skill acquisition and endurance are typical goals of physiotherapy exercise prescription. However, with the rise in prevalence of mental health conditions such as anxiety, it is important to acknowledge the additional benefits of exercise that extends beyond neuromusculoskeletal wellbeing.

Exercise dosage refers to measuring exercise exposure in frequency, intensity and duration (Physical Activity Guidelines Advisory Committee Report, 2018). Frequency refers to the rate of exercise performed over a period of time. Intensity points out the vigour or force with which exercise is performed. Duration implies the length of a single session of exercise. These three categorically refer to exercise dose. Types of exercise can broadly be described as strength training, endurance or aerobic training and high-intensity interval training.

The primary aim of this report is to map the data related to exercise in the management of GAD in adolescents and youth populations, thereby adopting an expansive approach to the information acquisition process. Thus, the use of a scoping review methodology aimed to decrease the constraints placed on the types of literature to consider, within the inclusion criteria, and produce a larger variety of reported exercise interventions in the management of GAD.

1.2 Research question

What exercises and dosages are used in managing symptoms of anxiety in youths and adolescents with GAD?

1.3 Aim of research

The aim of the study was to explore, map and describe the use of exercise and its specific application to youth and adolescents living with GAD.

1.4 Objectives

The main objective of this scoping review is to determine the types and dosages of exercise intended to bring about anxiolytic effects in youths and adolescents with GAD.

1.5 Significance of the study

This study will serve to map, determine and describe the evidence available regarding exercise interventions and GAD in adolescents. The benefits of exercise for mental health have been well established, however, less is known about exercise as a part of a management program for GAD.

There is much literature on exercise for GAD, but this is for the adult population. Less is known about the dosages for adolescents and youth. Therefore, we need to determine the evidence regarding the exercise to adequately focus on NPI, especially in this population.

CHAPTER TWO:

Literature review

2.1 Introduction

The following chapter provides background on the physiological mechanisms involved in anxiety and the literature surrounding the effects of exercise on anxiety. Pubmed and ScienceDirect were the main databases searched for articles/literature to complete this literature review. Keywords and phrases used included “effect of exercise on anxiety”, “generalized anxiety disorder and exercise”, “HPA-axis and exercise”, “BDNF and exercise” and “physiological effects of anxiety”. The searches were restricted to data published from 2013 to 2023 and search parameters were augmented towards children, adolescents and young adults where possible. The critical appraisal tools are available for viewing in Appendix B.

2.2 Definitions and prevalence

The World Health Organisation (WHO) states that patients with GAD may present with symptoms including “nervousness, trembling, muscular tension, sweating, light-headedness, palpitations, dizziness, and epigastric discomfort” (WHO,1992). Children may often present with pain, headaches, gastrointestinal complaints and palpitations (Dillon-Naftolin, 2016).

According to the Diagnostic and Statistical Manual of Mental Disorders (DSM-5-TR), the persistent and uncontrollable worry associated with GAD needs to be accompanied by at least three of the following somatic symptoms: disturbed sleep, irritability, difficulty concentrating, muscle tension and restlessness to fulfil the diagnosis (American Psychiatric Association, 2013). Subclinical or subsyndromal GAD is referred to as Analogue Generalised Anxiety Disorder (AGAD) (Volz et al., 2022). Analogue generalised anxiety disorder differs from GAD in that it may be present from one to six months and should meet two out of three of the somatic anxiety symptoms (Volz et al., 2022; Ruscio et al., 2007).

Globally, the lifetime prevalence of GAD in adults is 3.7% and increasingly pervasive as countries develop modern industrialised economies (Ruscio et al., 2017). In juxtaposition, Mohammadi et al. (2020) found that living rurally may decrease the likelihood of developing GAD. The rate of GAD varies greatly depending on the country. For example, in Germany, the lifetime prevalence of GAD in children and adolescents is 0.3% but it is much higher (11%) in New Zealand (Mohammadi et al., 2020). The rates of anxiety increase with age (Pavlova et al., 2022; Mohammadi et al., 2020) and a study by Solmi et al. (2022), found that GAD has a peak onset age of 15.5 years.

Incessant anticipatory anxiety is a central symptom of GAD and may be responsible for the evolution and continuation thereof (Buff et al., 2017). When assessing anxiety in children and youth, it is important to consider what is characteristically age-appropriate versus pathological and maladaptive responses or behaviour (Babaev et al., 2018). Exhibition of certain fearful or anxious behaviours may be part of typical development in children.

2.3 Neurophysiology

2.3.1 Anxiety circuitry of the Amygdala

The amygdala, situated deep in the temporal lobes of the brain, is involved in processing anxiety-related information and is described as an important modulator of vigilance and affective processor (Marloes et al., 2012; Phelps and Ledoux, 2005). Excessive excitability of this region is a feature of anxiety disorders in response to perceived negatively charged stimuli (Babaev et al., 2018). Uncontrolled sensitization of the amygdala may result in dysfunction of the stress response and lead to disorders like depression or PTSD (Kloet et al., 2005; Mc Ewen, 2004). This hyperexcitability refers to the physiological process where the neurons in the amygdala need a lower action potential for neuronal firing via a process of hyperpolarization. This lowered stimulus threshold results in more frequent neuronal firing (Rosen and Schulkin, 2022; Rosenkranz et al., 2010).

The physical manifestations of GAD are products of cascading stimuli processing in the anxiety circuitry of the amygdala (Babaev et al., 2018). The excitation of the basolateral amygdala (BLA) specifically, affects specialised regions namely the hypothalamus, bed nucleus of the stria terminalis (BNST), dorsal vagal complex, and periaqueductal grey that produce motor and autonomic responses presenting physically as the aforementioned symptoms (Babaev et al., 2018). It is important to note that inhibitory neurons serve the function of modulating the excitation in the amygdala and ensuring that stimuli are interpreted correctly as either hostile or positive (Babaev et al., 2018).

An example of hyperexcitability of the anxiety circuitry of the amygdala is illustrated in an experimental study involving 19 participants with GAD and 19 healthy control participants, where threatening stimuli were administered while they underwent functional magnetic resonance imaging (fMRI) (Buff et al., 2017). They found that the participants with GAD had increased phasic activity in the amygdala and amplified amygdala response to threat, compared to a healthy control group concerning threat anticipation. They go on to postulate that these findings could be used as neurological biomarkers in GAD (Buff et al., 2017).

Marloes et al. (2010) showed in a randomised controlled trial the time-dependent effects of corticosteroids on selective attention and emotional interference. Hydrocortisone was administered in a double-blinded, placebo-controlled design at 10mg either at 75 minutes or 285 minutes before the 72 male participants observed neutral facial expressions into fearful or happy expressions while receiving an MRI scan. The study concluded that corticosteroids play a desensitizing role in the amygdala's response to emotional stimuli. One of the theories for this finding is that the administered corticosteroid reduces the levels of circulating Corticotroph-releasing hormone (CRH). This hormone controls the activation of the central stress response (as will later be described) and can activate the amygdala thereby producing anxious behaviours. One of the deductions of this study is that decreased levels of circulating CRH is protective against excessive excitability of the amygdala.

2.3.2 Hypothalamic-pituitary-adrenal (HPA) axis

Elevated cortisol is part of a typical response to events such as waking up, exercising and sexual intimacy (Spencer and Deak, 2017). Cortisol is the main circulating hormone in the Hypothalamic-pituitary-adrenal axis, and HPA dysregulation is associated with mental health disorders (Spencer and Deak, 2017). Hypothalamic pituitary adrenal axis activation is also a result of stressful events and the ability to regain homeostasis following the event is crucial in stress management (Funke et al., 2016).

The HPA-axis neuroendocrine system controls glucocorticoid hormone production and secretion (Spencer and Deak, 2017). This system has three components namely the hypothalamus, pituitary gland and adrenal cortex. Corticotroph-releasing hormone (CRH) is secreted from neurons originating from the paraventricular nucleus of the hypothalamus and is necessary for the production and secretion of adrenocorticotropic hormone (ACTH) (Spencer and Deak, 2017; Faravelli et al., 2012). Corticotroph-releasing hormone neurons also produce Arginine Vasopressin (AVP), especially after chronic stimulation resulting in the simultaneous secretion of CRH and AVP (Spencer and Deak, 2017; Faravelli et al., 2012). Adrenocorticotropic hormone then causes the conversion of cholesterol to cortisol in the adrenal cortex (Spencer and Deak, 2017). The HPA axis is modulated by a feedback system involving mineralocorticoid and glucocorticoid receptors that control the amount of circulating cortisol to regain homeostasis (Stephens and Wand, 2012).

An author's manuscript by Herman et al. (2016) reported that women show greater HPA-axis stress-induced activity than that of men and that increased oestrogen states in women are linked to decreased circulating cortisol levels. This study also reports that the HPA-axis stress response is exaggerated in puberty when compared to adults regarding ACTH and glucocorticoid release and that these observations are part of normal development.

Funke et al. (2016) showed that a small group of GAD patients with comorbid depression, aged between 10-17 had increased morning cortisol levels in their saliva and plasma, and increased daytime salivatory alpha-amylase (sAA) activity compared to a healthy control group. Salivatory alpha amylase serves as an indication of the central nervous system's sympathetic state (Funke et al., 2016; Ehlert et al., 2006). The

authors recommended that a third participant group of depression only would have been beneficial to show the correlation or difference of the effects between anxiety and depression.

2.3.3 Brain-derived neurotrophic factor

Brain-derived neurotrophic factor (BDNF) has a multitude of functions ranging from neurogenesis, neural plasticity and stress resistance to glucose and energy metabolism (Miranda et al.,2019; Bethina and Das, 2015;). Changes in the levels of this neurotrophin are also associated with psychological disorders (Endstrom et al., 2008).

Brain-derived neurotrophic factor is classified as a neurotrophin and is expressed in the endoplasmic reticulum of neurons and glia (Bathina and Das, 2015). It is then transcripted, translated and cleaved (either intra-or extracellularly) and transported to the axon terminals and dendritic compartments (Miranda et al., 2019; Bathina and Das, 2015). Brain-derived neurotrophic factor is abundantly expressed with the highest concentration of BDNF found in the hippocampal neurons (where it acts pre-and post-synaptic and is involved with long-term potentiation), while also showing high levels in the amygdala, cerebellum and cerebral cortex, and low levels in multiple viscera such as the heart and lungs (Miranda et al., 2019; Leal et al., 2014).

An observational study by Carlino et al. (2015) compared the serum BDNF levels in adult participants, of which 252 participants had anxiety disorders and 420 were healthy participants. No relationship was found between serum BDNF levels and the severity of anxiety symptoms of patients with GAD, social phobia, panic attack disorder or specific phobia. They did however find that the female population with GAD had a statistically significant decrease in serum BDNF compared to the healthy control group and males. A cohort study by Molendijk et al. (2012) also found no statistical difference in BDNF levels across different anxiety subtypes (social anxiety disorder, panic disorder, agoraphobia and GAD) but that there was a decreased BDNF levels in females with anxiety disorders compared to the healthy control group. Molendijk et al. (2012) reported on two other studies with conflicting results by Kobayashi et al. (2005) and Strohle et al. (2010). The latter found that participants with panic disorder had lower

BNDF levels than the control group. This study had a small sample group of 12 participants of which nine were women. Molendijk et al. (2012) go on to suggest that the results may have been influenced by the larger percentage of females.

2.4 Exercise

In 2020, the World Health Organisation (WHO) released new guidelines for physical activity and exercise that they have categorised to broadly address all people in every stage of life. Concerning the populations covered in this review, the following guidelines are applicable. The WHO suggest that children and adolescents aged five to 17 years are to have at least 60 minutes of moderate to vigorous activity daily that is mostly aerobic. Additionally, this group should do activities that promote bone and muscle strengthening at a minimum of three days per week. These guidelines are applicable in the presence of disability too. Adults aged 18-64 are advised to perform 150-300 minutes of moderate to vigorous activity that is mostly aerobic in nature, or 75-150 minutes of vigorous aerobic type of exercise on a weekly basis. Additionally, general strengthening of the major muscle groups should be performed on two or more days a week for additional health benefits (WHO, 2020).

Regular exercise has a wide range of benefits that include but are not limited to improvement in cardiovascular health, mental and cognitive health, improved cardiometabolic health and reduction in the incidence of specific cancer (bladder, breast, colon, endometrial, oesophageal adenocarcinoma, gastric and renal cancers) (WHO, 2020).

A small experimental study by Dourida et al. (2018) involving eight male and four female adult participants, aimed at assessing the effects of a once-off bout of aerobic exercise on the acute hormonal response of the HPA-axis. A 30-minute bout of aerobic exercise was performed on a treadmill by these healthy participants at 70% of VO2 max. Measurement of resting ACTH, renin, cortisol and aldosterone was taken at rest, before commencing exercise and 30 minutes after cessation of exercise. The study found a statistically significant decrease in ACTH and cortisol after 30 minutes of exercise compared to baseline levels. The small sample size and lack of a control group weaken

this study, but it alludes to the modulating effects that aerobic exercise has on the HPA-axis.

A quasi-randomised study by Hotting et al. (2016) assessed the acute effects of exercise on memory, BDNF and cortisol in young adults. The study included 81 healthy male and female participants with a mean age of 22 and randomised them among high-intensity, low-intensity and relaxing groups. After their memory task, the exercising groups were asked to perform a single bout of 30 minutes on a cycling ergometer at less than 57% (low-intensity) VO2 max or up to 80% (high-intensity) VO2 max depending on their group. Blood samples for BDNF and saliva samples for cortisol were taken at three different times: baseline, after learning and after exercise. An increase in BDNF was noted in the high-intensity exercise group and the highest level of BDNF increased was directly after exercise. Cortisol levels increased with the intensity of exercise performed and were at their highest measurement at 20 minutes after exercise. This study shows the use of higher-intensity exercise modalities in the increase of BDNF and cortisol levels. It is important to note that these findings are in healthy, young individuals.

A systematic review by de Menezes-Junior et al. (2022) showed the effect of exercise modalities including treadmill running, Taekwondo, and resistance training on BDNF levels. This review included 11 articles where participants were healthy children and adolescents between the ages of eight and 19. The duration of exercise interventions ranged from one week to six months. Frequency ranged from three to seven days a week. An increase in BDNF levels in formally sedentary adolescents after short-term exercise was found. Higher levels of BDNF were found in plasma compared to serum samples in adolescent athletes compared to their sedentary counterparts. Very low correlation was found between physical activity levels for girls and their BDNF levels. The data sheds light on possible sex differences and base level activity levels for consideration with the impact of exercise on BDNF levels.

A small systematic review by Barahona-Fuentes et al. (2021) assessed the effect of different modes of strength training on adolescent stress, anxiety and depression. Six out of seven studies reviewed strength training's effects on anxiety levels and found it beneficial. Various forms of strength training were employed in these studies, encompassing high-intensity interval training (HIIT), the resistance training program for

CrossFit teens, whole-body vibrations combined with resistance exercise, and concurrent resistance-aerobic training. The duration of these interventions ranged from four to 22 weeks and was performed at a frequency of once to five times per week. They concluded that all types of strength training included in the study decreased levels of anxiety and depression.

Ramos-Sanchez et al. (2021) did a meta-analysis on the anxiolytic effect of exercise on anxiety disorders in adult participants with GAD, post-traumatic stress disorder (PTSD), panic disorder (PD), obsessive-compulsive disorder (OCD) or a combination of these disorders. The included 13 studies used aerobic exercise, resistance exercise or a combination of both modalities compared to control groups. This study found the effect size of exercise on symptoms of anxiety to be moderate (SMD 0.425). The included studies had durations of three to 20 weeks, frequencies ranged from one to five days a week and session lengths lasted from 16 to 90 minutes.

Gordon et al. (2017) conducted a meta-analysis consisting of 16 studies, to assess the effect of resistance exercise on anxiety in adult participants living with mental or physical illness. The illnesses included breast cancer, ischemic stroke, COPD, knee pain, obese adolescents, polycystic ovarian syndrome and GAD. The intervention duration ranged from two to 36 weeks and the frequency ranged from two to five days a week. They concluded that resistance exercise training had a small to moderate statistically significant effect on anxiety in both participants with physical and mental illness. Only one of the 16 studies included participants with GAD. The authors also neglected to specify the specific strengthening exercises used in the methodology.

The data presented confirms that exercise plays a positive role in the improvement of anxiety symptoms and the underlying physiology, whether in healthy or clinically anxious populations. Resistance and aerobic type exercise were the preferred modalities used in either the experimental or reviewed studies. This may be due to the ease of application or lack of exercise prescription knowledge. Sex differences in the presentation of anxiety symptoms and the impact of exercise on males versus females seem to be an important distinction that needs to be drawn as the differences in physiological presentation came to light in the completion of this literature review (Herman et al., 2016; Calino et al., 2015). Exercise could serve as an adjunct or interim

management tool for patients with anxiety disorders. Upon reviewing the literature, a lack of evidence in the field of exercise for managing anxiety symptoms in adolescents and youths became evident. The following section will present the data for this review on exercise in the management of GAD in adolescents and youths.

CHAPTER THREE

This chapter discusses the methodology employed and specifics regarding the search strategy, screening and reviewing, and data extraction.

3.1 Methodology

3.1.1 Study design

This scoping review was performed using the Joanna Briggs Institute methodology for scoping reviews. An ethical waiver was applied for and approved on 31/05/2022 (Appendix C). The ethics waiver registration number is W-CBP-220531-01. The scoping review was registered on open science framework, registration number: osf.io/4qa8e

3.1.2 Sample

The Population, Concept and Context framework was used to determine the inclusion criteria.

Population

Participants with a primary diagnosis of GAD were included in this review. All genders, from the age of 10-24 were included. The population in this age category are referred to as adolescents and youths. The WHO defines adolescents as individuals between the ages of 10-19 and the United Nations defines youth as people aged 15-24 (UN, 2012). Both these definitions were included to because individually the only partly include the target cohort.

Studies that depicted GAD as a secondary diagnosis to another specific medical condition were excluded. All other subcategories of anxiety where excluded. All studies that did included participants below age 10 and above age 24 were excluded.

Concept

The points of interest were the variation, frequency and intensity of exercise in the management of adolescents and youth diagnosed with GAD.

Context

This review considered all studies with participants between the ages of 10-24 years old where GAD was the primary diagnosis and exercise was used as an intervention in the management, irrespective of pharmacological or cognitive behavioural management.

3.2 Search strategy

An initial search was conducted on two databases namely Pubmed and ScienceDirect to locate studies on exercise as a treatment for GAD in adolescent and youth populations. The keywords and phrases in the logic grid (table 3.1) were adapted to suit the databases' advanced search tools and locate appropriate published data on the research topic. It was determined that the keywords and phrases in the Logic grid should exclude 'dosage' as this limited the number of search results without making those data more suited to the search. An advanced search was performed in Pubmed using the keywords in all texts (including title/abstract), MeSH terms and Text Word (Table 3.2).

Table 3.1: Logic grid organising keywords for the search of databases:

Terms connected by **OR**	**AND**	Terms connected by **OR**	**AND**	Terms connected by **OR**
Generalized Anxiety Disorder		**OR** Adolescent **OR** Youths **OR** Teenagers **OR** Child **OR** Juvenile		**OR** Aerobic exercise **OR** Exercise intervention **OR** Strength training **OR** Resistance exercise **OR** Yoga **OR** Sport **OR** HIIT **OR** Running **OR** Walking

Table 3.2 Search terms organised for Pubmed in Text word and MeSH Terms where available

Search Terms	MeSH Terms	Text Word
"Generalized anxiety disorder" [Title/Abstract] "Adolescent" "Teenager" "Youth" "Juvenile" "Child" "Exercise" "Aerobic exercise" "Exercise intervention" "Strength training" "Resistance training" "Yoga" "Sport" "HIIT" "Running" "Walking"	"Generalized anxiety disorder" "Adolescent" "Teenager" "Exercise" "Aerobic exercise" "Resistance training" "Yoga"	"Generalized anxiety disorder" "Adolescent" "Teenager" "Youth" "Juvenile" "Child" "Exercise" "Aerobic exercise" "Exercise intervention" "Strength training" "Resistance training" "Yoga" "Sport" "HIIT" "Running" "Walking"

To construct a comprehensive search, we used Boolean operators to combine the Text Word and MeSH terms. The Boolean logic used for Pubmed was as follows:

"generalized anxiety disorder"[Text Word] AND ("Adolescent"[MeSH Terms] OR "teenager"[Text Word] OR "youth"[Text Word] OR "juvenile"[Text Word] OR "child"[Text Word]) AND ("Exercise"[MeSH Terms] OR "aerobic exercise"[Text Word] OR "exercise intervention"[Text Word] OR "strength training"[Text Word] OR "resistance training"[MeSH Terms] OR "resistance exercise"[Text Word] OR "yoga"[MeSH Terms] OR "sport"[Text Word] OR "HIIT"[Text Word] OR "running"[Text Word] OR "walking"[Text Word] OR "yoga"[Text Word] OR "Exercise"[MeSH Terms] OR "Exercise"[Text Word])

In ScienceDirect an advanced search was performed with the following Boolean logic: “(Generalized anxiety disorder) AND (exercise intervention OR strength training OR resistance training OR resistance exercise OR yoga)”. This search was performed under title, abstract or author-specified keywords tabs. MeSH terms were not available on this database.

In the second phase of data sourcing, all included databases were searched namely PEDro, Cochrane database of systematic reviews and Cinahl Ultimate (Figure 3.2). These results were combined with the results of Pubmed and ScienceDirect from the initial search. Grey literature was searched for in Grey Literature Report, Worldcat, Grey Matters, ClinicalTrials.gov and Opengrey.

The searches were performed using variations of the following terms: Generalized anxiety disorder, anxiety disorder, aerobic exercise, exercise intervention, strength training, resistance exercise, yoga, sport, high-intensity interval training, running, walking, adolescents, youths, teenagers, child and juveniles. The keywords and phrases were adapted to each database and search engine for optimal refinement of search results and topic sensitivity. Search parameters were augmented towards children, adolescents and young adults where appropriate and available (Appendix A).

For additional data, all the references of the identified articles were consulted for possible additional articles that met the inclusion criteria. These additional studies were subjected to a title and abstract review, and where the eligibility of the article was unclear, a full-text review was performed. They were in- or excluded depending on the compatibility with the inclusion criteria.

3.3 Data charting

The results from the databases and search engines were exported and consolidated within a Microsoft Excel workbook. A link to these screening documents is available in Appendix C. A librarian at the Witwatersrand Health Sciences library was consulted in the search. Two reviewers independently screened and extracted data. The findings were discussed at each stage and any discrepancies were discussed and resolved between the two reviewers.

Each article was organized under the article title, authors, year of publication, database, citation, URL, and abstract if available from export results. Duplicate results were manually screened for and checked using the Excel program, identified and removed.

3.4 Screening and reviewing

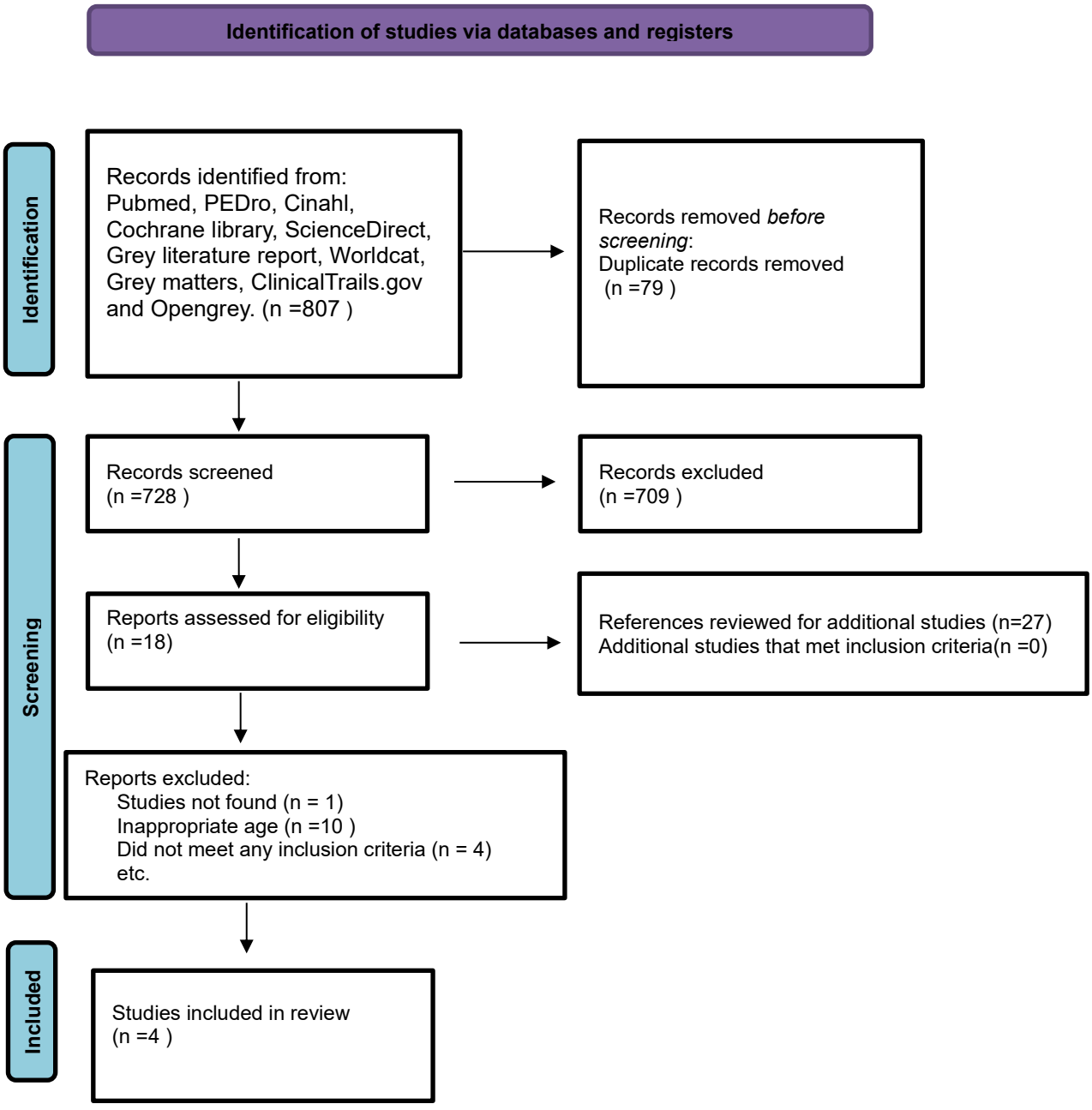
The initial screening process was conducted by two independent reviewers. The titles and abstracts of the results were reviewed for suitability. A full-text review was performed if it was unclear that the data in question was suitable for inclusion by their abstract and title alone. A list of the most appropriate results was then compiled, and the articles' full text was reviewed for eligibility to be included. Any disagreements were discussed between the two reviewers, who were able to reach agreement between them.

The search strategy results are presented in chapter four, via the Prisma flow diagram, Figure 3.2 (Page MJ et al., 2021). The characteristics of the gathered data, along with the refinement process and determination of their eligibility for inclusion or exclusion, are outlined in the following chapter.

CHAPTER FOUR

The ensuing chapter presents the data collected in accordance with the study parameters and methodology detailed in the preceding section.

Figure 4.1: Prisma flow diagram illustrating results of search (Page MJ et al., 2021)



4.1 Results

The searches resulted in 807 articles. After the removal of 79 duplicates, 728 articles remained. The titles and abstracts of these articles were reviewed for eligibility with a second reviewer and 18 articles were found appropriate for a full-text review. Following the review of the full text, a further 14 studies were excluded. These studies were excluded from the study for various reasons, including inappropriate age for the target population (n=10), no exercise or GAD included in the article (n=3), and the study itself not being found (n=1). The results amounted to a total of four articles that met the required inclusion criteria of this review (figure 4.1).

To gather more data, we examined the references of the original 18 articles to find additional articles that fit our inclusion criteria, as well as the references of the four included studies. This process led to the discovery of 27 more studies, which underwent a review of their titles and abstracts. If the eligibility of an article remained uncertain, we examined its full text. However, no further studies meeting the inclusion criteria were found through this reference search. There were no disagreements between the reviewers related to studies selected for inclusion, thus consultation with a third reviewer was not necessitated. Table 4.1 documents the information that was extracted from the included articles. The data has been directly copied to minimise bias.

One study was found in the grey literature of which 20 participants, in a total of 30, fell in the youth age range. This study by Herring M.P. (2010) explored resistance-type exercise in the form of lower body strength training and dynamic leg cycling as aerobic training, at a frequency of twice a week to address the symptoms of GAD. The intervention duration was six weeks. For inclusion in this study, the participants underwent diagnostic interviews which resulted in the diagnosis of GAD according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV). Three more studies were conducted involving participants diagnosed with Analogue generalized anxiety disorder (AGAD) (Flemming et al., 2020; Herring et al., 2019; Herring et al., 2017). These three studies were produced by the same authors, the details of which are outlined in Table 4.1. The diagnosis of AGAD was reached when the participants had a score of 45 or higher on the Penn State Worry Questionnaire (PSWQ). In a pilot study,

Herring M.P (2017) used the dosage of a single bout of vigorous treadmill running for the duration of 30 minutes to address symptoms of worry, trait anxiety, depressive symptoms, and sleep quality. Herring et al. (2019) went on to describe the effect of the same kind of aerobic type intervention, namely treadmill running for 30 minutes, in a study involving 19 male and 16 female participants. These participants were diagnosed with AGAD following the completion of PSWQ and scored 45 or higher. This study explored if the effect of vigorous treadmill running on the symptoms of worry, trait anxiety, depressive symptoms, and sleep quality may differ between the two sexes. Lastly, Fleming et al. (2020) investigated what effect a single bout dosage of 30 minutes of beginner Pilates would have on 87 young males with AGAD.

It is not within the scope of this review to report on methodological quality. Subsequent concluding chapters will delve into the results, particularly concerning exercise dosage, and outline potential gaps in the literature.

Table 4.1: Data charting								
Authors	Year	Aim	Sample size	Sex	Diagnosis	Exercise type	Frequency	Duration
Herring MP	2010	"The purpose of this study is to compare the effects of 6 weeks of endurance or strength training and a wait list comparison condition on symptoms of Generalized Anxiety Disorder (GAD)."	30 participants 18-39 years (20 between 18-23 years)	Female	GAD	1) Lower-body strength training progressing from 50% to 75 % predicted one-repetition maximum. 2) Dynamic leg cycling matched to the strength training arm on total positive work completed, total time actively engaged in exercise and weekly load progression. 3) Waiting list control group	2 weekly sessions"	6 weeks
Herring MP, Hallgren M, Campbell MJ	2017	"The authors hypothesized that, compared to quiet rest, an acute bout of aerobic exercise would significantly improve worry, state anxiety, and feelings of energy and fatigue among young women with worry indicative of GAD." Pg 5	17 participants Mean age 20.8 ± 1.4 years	Female	AGAD	"i) 30-min of vigorous running on a treadmill, or ii) 30-min seated quiet rest" Pg 6	-	"a vigorous (Committee, 2008) 30-min supervised bout" Pg 8
Herring MP, Monroe DC, Gordon BR, Hallgren M, Campbell MJ	2019	"The authors hypothesized that, compared to quiet rest, an acute bout of aerobic exercise would significantly improve worry, state anxiety, and feelings of energy and fatigue among young adult women and men with worry indicative of GAD." Pg 3	35 participants Mean age 21.4 ± 2.3 years	19 males 16 females	AGAD	"a vigorous (20) 30-min supervised bout of running on a Woodway Pro© treadmill at 65% to 85% of maximal HR reserve (%HRR)." Pg 4	-	"a 30-min bout of treadmill running" Pg 7
Fleming KM, Campbell M, Herring MP	2020	"the key objective of the study reported here was to examine the effects of a single bout of Pilates on state anxiety, worry, and feelings of tension, depressed mood, energy and fatigue, and total mood disturbance among young adult males with no Pilates experience." Pg 2	87 participants Mean age 19.3 ± 3.1 years	male	AGAD	"Four repetitions of each Pilates movement, outlined in the sequence of mat based beginner's exercises (Table 1), were performed during the 30- minute session." Pg 2	-	"A single-arm pre-post-acute intervention" Pg 2

CHAPTER FIVE

5.1 Discussion

This review aimed to present the extent of literature on exercise dosages and types, in the management of adolescents and youths with GAD. The results showed that very few studies (n=4) concerning exercise management or interventions, in the adolescent and youth age group with a diagnosis of GAD, have been conducted.

The four sets of data outlined in the results included one study that had a duration of six weeks and a frequency of twice a week (Herring, 2012), while the three remaining studies discussed the effects of the dosage of a single bout of exercise (Flemming et al., 2020; Herring et al., 2019; Herring et al., 2017). Flemming et al. (2020) incorporated a single bout of Pilates and reasoned that this was necessary as it was yet inconclusive what acute effects may be brought about on mood states by Pilates. Herring et al. (2017) set out to test the acute effects of exercise in young women and thus a frequency of a single bout was deemed most appropriate to their pilot study. They also determined if effects differed regarding their AGAD, depression or physical activity levels. In 2019, Herring et al. replicated the 2017 study but included young men in their cohort to explore sex-related deviation and ascertain if the previous study results extended to the male population.

A single bout of high-intensity exercise certainly has been shown to increase BDNF levels and cortisol in healthy populations (Hotting et al., 2016) and the use of single-bout aerobic exercise showed favourable effects on the HPA-axis and BDNF levels (Dourida et al., 2018). This holds significance due to the established knowledge that females with GAD exhibit lower BDNF levels, as noted by Carlino et al. (2015) and Molendijk et al. (2012). Consequently, it reinforces the rationale for employing a single-bout duration of exercise as a supportive intervention. Another interesting aspect for consideration could be whether the duration of the exercise intervention had any influence on the duration of anxiety symptom improvement.

The types of exercises reported had a very narrow range, probably due to the small number of included studies, and that two of the studies simply replicated the intervention but changed the cohort. The types of exercise outlined were lower body strength

training and dynamic leg cycling as aerobic training (Herring M.P., 2010), vigorous treadmill running (Herring et al., 2019; Herring et al., 2017) and Pilates (Flemming et al., 2020). In the 2010 study by M.P. Herring, no particulars could be found informing his choice of exercise implemented. Flemming et al. (2020) chose Pilates as their exercise type, as they reported that less traditional forms of exercise like Pilates and Tai Chi, and their effects on mood states were understudied. Herring et al. (2019) selected vigorous treadmill running as their exercise modality, drawing upon their prior research that involved the implementation of acute aerobic exercise (Herring et al., 2017; McDowell et al., 2016). The pilot study by Herring et al. (2017) implemented the 30-minute bout of vigorous treadmill exercise as outlined in the McDowell et al. (2016) study which demonstrated the positive effects of this intervention on mood.

Aerobic exercise and various types of strength training have demonstrated positive effects on anxiety symptoms across anxious and depressed adolescents, adults with anxiety disorders and healthy populations (Barahona-Fuentes et al., 2021; Ramos-Sanchez et al., 2021; Dourida et al., 2018). It is important to note that Hotting et al. (2016) also found that cortisol levels increased for at least 20 minutes following higher-intensity exercise in young adults. This needs consideration if it is recognised that this particular cohort may have difficulty with returning the HPA-axis to homeostasis. Additionally, increased levels of salivatory cortisol levels and sympathetic arousal have been found in patients with GAD (Funke et al., 2016). These physiological presentations may help inform the choice of exercise appropriately for its desired physiological outcome. For instance, as demonstrated by Dourida et al. (2018), engaging in a 30-minute session of aerobic exercise resulted in a decrease in cortisol levels. Aerobic exercise may be beneficial in assisting in modulating the amygdala, as Marloes et al. (2010) infer that decreased levels of circulating CRH aid in decreasing the affective response of the amygdala. Studies including females may need to consider their phase in the menstrual cycle as Herman et al. (2016) found decreased circulating cortisol with increased states of oestrogen. Therefore, understanding and accounting for these hormonal variations are essential for the effectiveness and accuracy of the intervention.

Regarding BDNF levels, increases were seen with vigorous high-intensity exercise, aerobic exercise, strength training, and taekwondo (de Menezes-Junior et al., 2022) in

healthy adolescents. Though Carlino et al. (2015) found no correlation between the severity of anxiety symptoms and BDNF levels it is noteworthy that this same study found decreased BDNF levels in females with GAD. That said, with all we know about the physiological effects of different exercise modalities and the physiological presentation of GAD, the included data seemed to have based their choice of intervention on the fact that exercise is an anxiolytic. By adopting a more nuanced approach, they might have been capable of discerning the underlying factors contributing to the changes in the anxiety symptoms rather than merely assessing whether improvement occurred.

None of the included studies resembled the WHO guidelines for exercise duration of at least 60 minutes with daily frequency (WHO, 2020), which closely resembled the Recommended Population Levels of Physical Activity for Health (WHO, 2010), which the authors of the earliest included article and subsequent publications should have had access to. This is probably because these parameters didn't align with the author's study objective.

In contrast to the included results, at least 16 studies were noted from the original search results regarding GAD and exercise for the management thereof, in adults. The fact that more results were obtained for adults, using a very specific search strategy geared towards youths and adolescents, points to a definite lack of literature in the adolescent and youth age group. Of those, seven studies reported on different disciplines of yoga (Simon et al., 2021; More et al., 2021; Bukar et al., 2019; Gabriel et al., 2018; Hoffman et al., 2015; Doria et al., 2015; Ranjbar et al., 2011), one study looked at HIIT (Plag et al., 2020), five studies discussed resistance and aerobic exercise (Gordon et al., 2021; Wang et al., 2019; Herring et al., 2012; Herring et al., 2011; Herring et al., 2010), one study reported on breathing exercises (Maleki et al., 2022) and one on a home-based walking program (Merom et al., 2008). Frequencies varied from weekly sessions to three times a week and durations ranged from one week to six months. Generally, no justification is given for the duration or frequency of the exercise interventions. Reasons for the choice of exercise intervention range from its efficacy in reducing GAD symptoms; efficacy compared to CBT, stress education or other types of exercise and the psychological effect of certain exercise types.

The likelihood of encountering a greater variety of exercise types in studies involving adult participants, as opposed to those involving adolescents and youth, could stem from the relatively fewer barriers associated with recruiting adults for research participation. Rice et al. (2018) described possible barriers to the recruitment of children in research. These barriers range from complicated recruitment strategies and layers of communication needed to gain approval from schools or clinic staff before gaining access to parents for consent to recruit children into studies. Other barriers such as cost of participation (financial or travel difficulties), schedule disruptions, stigma surrounding disclosure of a child's diagnosis, incentives needed to keep appointments and lack of information on the research process on behalf of the child, all play a role in creating difficulties with recruitment of children into research.

The included studies did satisfy the review question, however, only the upper age parameter was available in the data included in this review. None of the results included participants aged 10-18 years. This points to a gap in the literature for the exploration of different types and dosages of exercise in the adolescent and youth age bracket.

Though it is important to have inclusive data regarding the management of specific anxiety disorders with exercise across different stages of life, it should be of particular interest and importance to study specifically younger populations, as it is known that anxiety disorders can have an age of onset as young as five years old (Solmi et al., 2022).

CHAPTER SIX

6.1 Conclusion

The results of the review were unexpected but present ample opportunity for further exploration of this topic of exercise management with younger participants living with GAD. The main speculated reason for the lack of data is possible barriers that exist with recruiting children and youths into research programs. The lack of data available warrants further, especially in the NPI arm of treatment, other than CBT, for children and youths living with GAD.

Much is known about the physiological and anxiolytic effects of exercise and the specific presentation of anxiety mechanisms and disorders, as well as gender-specific physiological variations. It seems that future research must include a multi-disciplinary approach including exercise specialists, psychologists and physiologists, to formulate objectives that encourage investigation of bespoke interventions. The lack of overlap in these specialist disciplines could result in a considerable delay in bridging the gap between research and practical implementation.

6.1.1 Strengths and limitations

Only the upper age parameter was available in the data for inclusion in this review. None of the results included participants aged below 18 years. A possible limitation of this scoping review is that it looked at GAD in isolation, which is important, but adding anxiety subtypes to the literature search may have yielded more search results in the applicable age range. By employing the scoping review methodology without limiting the search to specific publication years, we conducted an extensive exploration of the existing literature. This approach facilitated an unrestricted investigation into the research conducted regarding GAD and exercise in adolescents and youth, offering a comprehensive overview of the extent of available studies.

6.1.2 Future recommendations

It is recommended that more research be done in these younger age groups and that efforts should be made to draw distinctions between the different anxiety diagnoses when reporting and discussing findings, especially due to the increasing prevalence of anxiety in children and adolescents. Future studies could investigate the impact of exercise on the treatment of GAD, with a focus on understanding potential variations between genders as literature has suggested that women exhibit higher levels of HPA-axis stress-induced activity compared to men (Herman et al., 2016). Additionally, it would be valuable to explore suitable forms of exercise for adolescents and youths, aiming to promote anxiety relief by moderating the HPA-axis, as Herman et al. (2016) report that the HPA-axis stress response is exaggerated in puberty when compared to adults, though it is a part of normal development. An intriguing avenue for research would involve a study where the intervention is guided by scientifically supported dosages and tailored to the specific physiological effects of each type of exercise to address the physiological presentation of GAD and assess its effectiveness.

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7: APPENDICES

APPENDIX A: Search strategies

1. Pubmed

Keywords searched in all texts (including title/abstract) and MeSH terms.

Search	ID	Results
(Generalized anxiety disorder[Title/Abstract]) OR (Generalized anxiety disorder[Text Word])	#1	9,241
(((((((adolescent[MeSH Terms]) OR (teenager[MeSH Terms])) OR (youth[MeSH Terms])) OR (Adolescent[Text Word])) OR (teenager[Text Word])) OR (youth[Text Word])) OR (juvenile[Text Word])) OR (child[Text Word])	#2	3,632,168
((((("Exercise"[MeSH Terms] OR "aerobic exercise"[Text Word] OR "exercise intervention"[Text Word] OR "strength training"[Text Word] OR "resistance training"[MeSH Terms] OR "resistance exercise"[Text Word] OR "yoga"[MeSH Terms] OR "sport"[Text Word] OR "HIIT"[Text Word] OR "running"[Text Word] OR "walking"[Text Word]) OR (yoga[Text Word])) OR (aerobic exercise[MeSH Terms]))) OR (exercise[Text Word])	#3	616,791
"generalized anxiety disorder"[Text Word] AND ("Adolescent"[MeSH Terms] OR "Adolescent"[MeSH Terms] OR "Adolescent"[MeSH Terms] OR "Adolescent"[Text Word] OR "teenager"[Text Word] OR "youth"[Text Word] OR "juvenile"[Text Word] OR "child"[Text Word]) AND ("Exercise"[MeSH Terms] OR "aerobic exercise"[Text Word] OR "exercise intervention"[Text Word] OR "strength training"[Text Word] OR "resistance training"[MeSH Terms] OR "resistance exercise"[Text Word] OR "yoga"[MeSH Terms] OR "sport"[Text Word] OR "HIIT"[Text Word] OR "running"[Text Word] OR "walking"[Text Word] OR "yoga"[Text Word] OR "Exercise"[MeSH Terms] OR "Exercise"[Text Word])	**#1 AND #2 AND #3**	46
Results		46

2. Cochrane

Keywords searched in title/abstract keyword and MeSH. No additional filters were applied.

Search	ID	Results
generalized anxiety disorder or GAD or anxiety disorder	#1	23178
exercise intervention aerobic training or strength training or resistance exercise or yoga or HIIT or sport	#2	89425
MeSH descriptor: [Exercise] explode all trees	#3	37900
child or adolescents or teenagers or teen or juvenile or youth	#4	209620
MeSH descriptor: [Adolescent] explode all trees	#5	125165
MeSH descriptor: [Child] explode all trees	#6	77476
#1 AND #2 AND #3 AND #4 AND #5 AND #6	#7	11
Results		11

3. Cinahl Ultimate via EBSCOhost

Keywords and phrases were searched in all text. No MeSH terms were not available.

Search	ID	Results
TX child or adolescents or teenagers or teen or youth or juveniles	S1	2004575
TX exercise or aerobic training or strength training or resistance exercise or yoga or HIIT or sport	S2	707094
TX generalized anxiety disorder or gad	S3	18096
TX S1 AND TX S2 AND TX S3	S4	2438
Filters applied to S4: English	S5	2407
Filters applied to S4: child: 6-12 years, adolescent: 13-18 years	S6	622
Result		622

4.PEDro (Physiotherapy Evidence Database)

Keywords: Generalized anxiety disorder and exercise searched in Title and abstract bar.

No other filters or parameters applied.

Search	ID	Results
Generalized anxiety disorder and exercise		23
Results		**23**

5. ScienceDirect

Advanced search performed with:

(Generalized anxiety disorder) AND (exercise intervention OR strength training OR resistance training OR resistance exercise OR yoga)" searched in Title, abstract or author-specified keywords tab.

MeSH terms were not available.

Results: 42

6. Grey literature:

Grey literature report (Greylit.org)

The following search was conducted in the search bar:

General anxiety disorder AND exercise intervention

Child or youth or teenager or juvenile were added in the additional keywords tab.

Results: 0

7. Worldcat

The following search was conducted under the advanced search:

Title: ti:(generalized anxiety disorder) AND

Keyword: kw:exercise NOT

Keyword: kw:adults

ti:(generalized anxiety disorder) AND kw:exercise NOT kw:adults

The search was refined by 'Format': Book: Thesis and dissertation checked,

Articles, Chapters: all checked.

Language refined to English only.

Results: 46

8. Grey matters:

The following search was conducted in the search bar:

Generalized anxiety disorder AND Aerobic exercise OR Strength training OR Yoga AND Adolescence OR Youths OR Teenagers OR child.

Results: 0

9. OpenGrey (via DANS EASY Data Archive)

The following search was conducted:

Generalized anxiety disorder AND Aerobic exercise OR Strength training OR Yoga AND Adolescence OR Youths OR Teenagers OR Child

Results: 0

10. ClinicalTrails.gov

The following search was conducted in advanced search:

Condition: Generalized anxiety disorder

Other terms:

Exercise intervention OR Strength training OR Resistance exercise OR Yoga OR Sport OR High-intensity training OR Running OR Walking AND Adolescence OR Youths OR Teenagers OR Young adult OR Juvenile

Status: Completed

Eligibility criteria: Age: Child 0-17 and Adult 18-64

Results: 19

Total results: 807 articles collectively

After removing duplications: 728 studies remained

APPENDIX B: ETHICAL WAIVER

UNIVERSITY OF THE WITWATERSRAND V JOHANNESBURG	HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

Office of the Deputy Vice-Chancellor (Research & Innovation)

TO: Ms N Leander
School: Therapeutic Sciences
Department: Physiotherapy
Medical School
University

E-mail: 22092030students.wits.ac.za

cc: Supervisor: Ms S Lord <Sandy.Lord@wits.ac.za>
and <HREC-Medical.ResearchOffice@wits.ac.za>

FROM: Mr lain Burns
Human Research Ethics Committee (Medical)
Tel: 011 717 1252

E-mail: lain.Burns@wits.ac.za

DATE: 31/05/2022

REF: R14/49

PROTOCOL NO: W-CBP-220531-01 (This is your ethics application study reference number. Please quote this reference number in all correspondence relating to this study)

PROJECT TITLE: Exercise dosages for the management of Generalized Anxiety Disorder: a scoping review

Please find attached the Ethics Waiver Certificate for the above project. I hope it goes well and that article in a recognized publication comes out of it. This will reflect well on your professional standing and contribute to the Government funding of the University.

UNIVERSITY OF THE WITWATERSRAND V 101 JOHANNESBURG	HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

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Office of the Deputy Vice-Chancellor (Research & Innovation)

31/05/2022

Ref: W-CBP-220531-01

TO WHOM IT MAY CONCERN

Waiver: This certifies that the following research does not require clearance from the Human Research Ethics Committee (Medical)

Investigator: Ms N Leander
Student No. (if appropriate): 2209203 Staff No. (if appropriate):

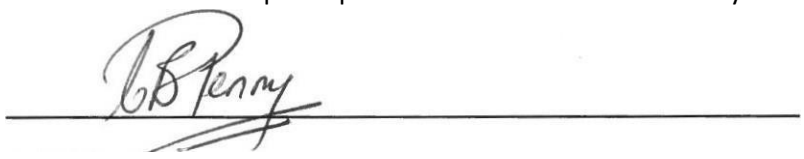
Supervisor: Ms S Lord

School: Therapeutic Sciences

Department: Physiotherapy
Medical School University

Project title: Exercise dosages for the management of Generalized Anxiety Disorder: a scoping review

Reason: Review of information in the public domain
No human participants will be involved in the study



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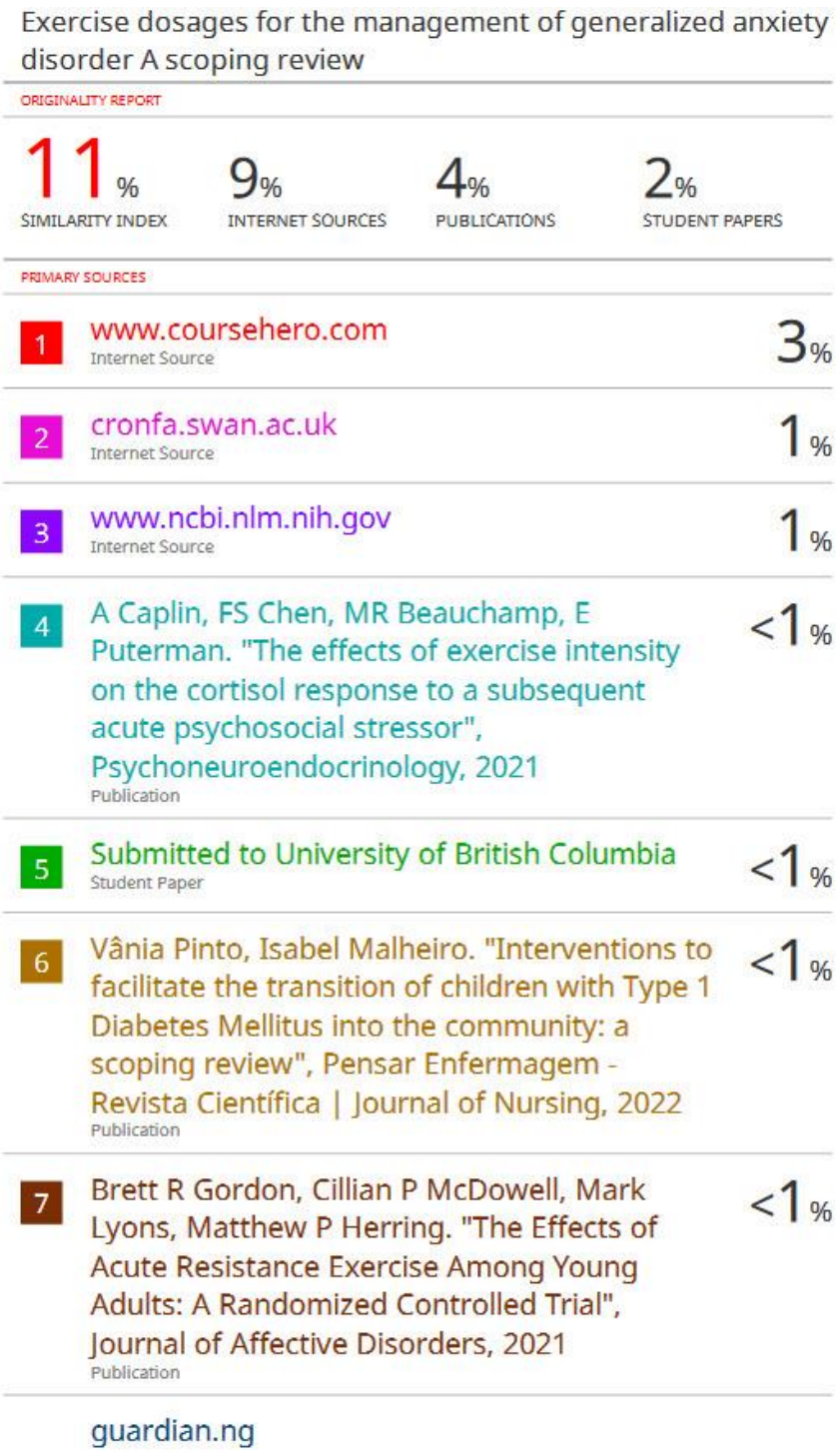
APPENDIX C: SCREENING DOCUMENTS

The following link is an Excel file containing four workbooks. Each of these workbooks illustrates a step in screening the search results obtained in the scoping review.

They are named Original, Duplicates removed, Full-text review and References for review, respectively. Their labels indicate the position in the screening continuum and what information they hold.

Screening and final search results.xlsx

APPENDIX D: TURNITIN REPORT



Exercise dosages for the management of generalized anxiety disorder A scoping review

ORIGINALITY REPORT

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