THE EFFECT OF BERGAMOT ESSENTIAL OIL ON ANXIETY AMONG CHILDREN WITH AUTISM

by

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ABSTRACT

The purpose of this study was to evaluate the effect of bergamot essential oil inhalation on anxiety scores of children with autism during routine medical visits, as measured by an anxiety inventory, heart rate, and blood pressure. Children with an autism spectrum disorder experience anxiety at rates much higher than children who do not have an autism spectrum disorder. There is a growing need for non-invasive solutions to the anxiety experienced by children with an autism spectrum disorder that are both safe and effective. This study evaluated the role of a sensory enhanced environment through the use of bergamot essential oil as a tool to improve both problem-focused coping and emotional regulation of children with an autism spectrum disorder who require routine medical visits.

The study consisted of a 15-minute exposure to bergamot essential oil at the start of the medical visit, once the child was in the medical examining room. The child’s blood pressure and heart rate, State Trait Anxiety Inventory for Children (STAI-CH) were taken at the start of the visit and again after 15 minutes of exposure to the oil. After adjusting for baseline scores, children who inhaled the bergamot essential oil during the 15 minute period had similar heart rate and blood pressure readings as children who did not inhale the bergamot essential oil.

Children who inhaled bergamot essential oil during the first 15 minutes of their medical appointments had anxiety scores which were similar to children who did not inhale the essential oil for the entire scale. When the portion of the inventory
which evaluated the absence of anxiety related feelings was evaluated, it was also found that children who inhaled bergamot essential oil during the first 15 minutes of their medical appointments had significantly higher scores than children who did not inhale the essential oil.

Based on the findings of this study, exposure to the essential oil during the first 15 minutes of a medical office appointment does not reduce anxiety scores in children who have autism and may even increase the perception of anxiety these children experience.
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CHAPTER 1: THE PROBLEM

Introduction to Autism Spectrum Disorders

Autism is a psychological condition which impacts individuals of all ages and is typically diagnosed in early childhood (CDC, 2016). There are multiple diagnoses which exist on the spectrum of autism disorders, all of which impact an individual’s ability to thrive in a social context. The term autism refers to a spectrum of “persistence deficits in social communication and social interaction across multiple contexts,” according to the Diagnostic and Statistics Manual, version 5 (DSM-V, 2013).

These deficits include social-emotional reciprocity, nonverbal communication, and relationships. Other symptoms include restrictive, repetitive patterns of behavior including an insistence on sameness and hyper- or hypo reactivity to sensory input (DSM-V, 2013). These symptoms impact more than social interaction, extending to discomfort and anxiety related to routine daily activities. There is no single cause or cure for autism, and interventions are focused on reducing the symptoms which inhibit quality of life for individuals living with an autism spectrum disorder (CDC, 2016).

History of Autism Spectrum Disorders

Autism burst onto the scene in the mid-1900s and appearing in the 1980 DSM-III, which included diagnostic criteria for infantile autism and for pervasive
development disorder (DSM, 1980). In the 1994 DSM-IV, the diagnosis was revised to include Asperger’s and a total of five diagnoses under the autism spectrum, and in the 2013 DSM V, autism diagnoses were consolidated to a single diagnosis of Autism Spectrum Disorder (ASD) with a range of three tiers (DSM-IV, 1994 & DSM-V, 2013). These tiers include level 1 “requiring support,” level 2 “requiring substantial support,” and level 3 “requiring very substantial support” (DSM-V, 2013).

Symptoms are diagnosed by observation as there are no laboratory tests to assess whether or not an individual has an ASD. These observable behaviors focus on social communication and interaction deficits in three specific areas: social-emotional reciprocity, nonverbal communicative behaviors, and the development, maintenance, and understanding of relationships (DSM-V, 2013). These behaviors may be demonstrated as an insistence on sameness in routine or schedule, intensely focused interests in a specific object or subject, hyper- and hyposensitivity to sensory stimuli, and difficulty in social interactions.

Diagnostic criteria evaluate the presence of this range of symptoms, as well as the severity of which these symptoms impact the ability to function in normal social settings. Practitioners evaluate the extent to which these symptoms inhibit or restrict social behaviors, and how these symptoms may be better explained by other diagnoses to arrive at an ASD diagnosis (DSM-V, 2013).
Epidemiology of Autism Spectrum Disorders

Autism was considered to be an extremely rare developmental disorder in the 1960s and 1970s; in the 1990s, incidence began to rapidly increase, and that growth continues today (CDC, 2016). In the 1980s, two prevalence studies found 3.3 and 3.6 cases per 10,000 children aged 3-18 years old (Ritvo et al., 1989). In the year 2000, the Autism and Developmental Disabilities Monitoring Network (ADDM) estimated prevalence to be 6.7 per 1,000 eight-year old children, and by 2012, that figure had grown to 14.6 per 1,000 eight-year old children, or approximately 1 in every 68 children (CDC MMWR, 2010 and 2014). Worldwide, this figure is 1 per 160 children, according to the World Health Organization (WHO, 2017). The worldwide figure is lower in part because prevalence from low- and middle-income countries is unknown and worldwide prevalence varies significantly.

Autism spectrum disorder is now so prevalent that the American Association of Pediatricians recommends that children should be screened twice for an autism spectrum disorder, once at 18 months of age and again at 24 months of age (Johnson & Myers, 2007). Healthy People 2020 has set a goal of having children screened for an autism spectrum disorder by the age of 36 months, with support services provided by the age of 4 years (Healthy People 2020). Healthy People 2020 Objective MICH 29.1 includes screening between 10 and 35 months, MICH 29.2 includes having a first evaluation by 36 months, and MICH 29.3 includes achieving access to special services by 48 months (Healthy People 2020).
According to the 2012 ADDM data, autism spectrum disorder prevalence is far greater among boys than girls. Male prevalence of autism spectrum disorder was 23.6 per 1,000 eight year old children, while female prevalence was found to be 5.3 per 1,000 eight year old children, with a total prevalence ratio for boys compared to girls of 4.5 (CDC, 2016). Autism spectrum disorder prevalence was also found to be higher among non-hispanic white children, and children from families with higher socioeconomic status (CDC, 2016).

**Burden of Autism Spectrum Disorders**

The rising prevalence of autism spectrum disorders are reflected in rising costs associated with direct medical expenses, non-direct medical expenses, and productivity. Individuals with an ASD are more likely to require special educational services than individuals who do not have an ASD (76% as compared to 7%), costing an average of $8,610 more in educational services each year (Lavelle et al., 2014). Care for each child with an autism spectrum disorder costs an average of $3,020 more each year in direct healthcare costs and $14,061 in non-healthcare costs (Lavelle et al., 2014).

Care for adults with an autism spectrum disorder can be even more expensive. Total direct, nondirect, and productivity costs of supporting an individual with an autism spectrum disorder are estimated to average $1.4 million for an autistic individual who does not also have intellectual disability and $2.4 million for an
individual who has both an autism spectrum disorder and intellectual disability (Buescher et al., 2014).

Nationally, the total direct, indirect, and productivity financial burden of autism is predicted to be $268 billion (range $162 billion to $374 billion) for the year 2015 (Leigh et al., 2015). At the upper end of that estimated range, the economic burden of autism accounts for 2% of the United States’ total GDP.

**Anxiety and Autism Spectrum Disorders**

According to the DSM-IV, an anxiety diagnosis for an individual with ASD required the presence of anxiety symptoms which cannot be explained exclusively through the ASD diagnosis (DSM-IV, 1994). This changed in the DSM-V, which identifies anxiety as a comorbid condition and simply requires that the symptoms are not *better* explained by the autism spectrum disorder diagnosis. Distinguishing between anxiety which exists as a symptom of an autism spectrum disorder and anxiety as a comorbidity is difficult and imprecise. This is reflected in a 2013 study which sought to identify relationships and moderating effects of ASD symptoms, and found that over 50% of the variance on total anxiety scores could be explained by autism spectrum disorder symptomatology (Reiske et al., 2013).

Children with an autism spectrum disorder experience both typical anxiety symptoms and atypical anxiety symptoms, which are behaviors that do not reflect DSM definitions. In one sample, 48% of children experienced traditional anxiety
disorders while 46% of children experienced anxiety symptoms which are not consistent with psychological disorders related to anxiety found in the DSM (Kerns et al., 2014). These symptoms include experiences such as anxiety related to changes in routine, social fearfulness, and ritualistic behaviors. Of the 46% of children who experienced atypical symptoms, 31% also experienced typical symptoms, demonstrating the overlap in symptomology among anxiety disorders and autism spectrum disorders.

These anxiety symptoms can be predicted by variables related to ASD traits. Children with ASD who are verbal, who have an IQ over 70, and who also have related symptoms such as hyperactivity and irritability are more likely to score higher on anxiety scales than children without those traits and related symptoms (Hallet et al., 2013). When researchers evaluated ASD traits and experiences which predict various anxiety related behaviors, 58% of the variance in social anxiety was predicted by autistic traits, with social competence as the symptom having the largest effect (Liew et al., 2015). Other factors which contributed to the overall experience of anxiety include social problem solving, adverse sensory experiences, prevention from/punishment for preferred repetitive behaviors, and teasing in social experiences.

**Epidemiology of Anxiety Among Children with an ASD**

Among children who have an autism spectrum disorder, anxiety is the most common comorbidity, with prevalence of anxiety-like symptoms ranging from 11% to
84%, depending on the study (Williams et al., 2015). Approximately 40% of children who have an autism spectrum disorder receive at least one formal diagnosis of an anxiety related disorder according to multiple prevalence studies (van Steensel et al., 2011). These figures are staggering compared to the general population, with anxiety prevalence figures ranging from 2.2% to 2.7% (Costello et al., 2005).

Anxiety disorders experienced by children with an autism spectrum disorder vary. In a meta-analysis evaluating which type of anxiety disorders are experienced by individuals with ASD, specific phobia was the most prevalent at nearly 30%, and obsessive-compulsive disorder and social anxiety disorder each presented in approximately 17% of cases (van Steensel et al., 2011). Anxiety is more prevalent in males than females, but when specific symptoms of anxiety are evaluated, males demonstrate symptoms of hyperactivity while females exhibit symptoms of social anxiety (May et al., 2014).

Autism spectrum disorder and anxiety comorbidity also increases the overall economic burden of health care related expenses both individually and as a society. Overall healthcare expenses for children who have both an autism spectrum disorder and anxiety related disorders are approximately four times higher than autism spectrum disorder diagnoses alone, and approximately 27 times higher than expenses for individuals who have neither an autism spectrum disorder nor anxiety (van Steensel et al., 2013).
Other Comorbidities

Autism spectrum disorder is a psychological diagnosis, but individuals with an autism spectrum disorder experience comorbidities with a wide range of symptoms. Children with ASD experience sleep disorders, metabolic disorders, immune dysregulation, cytokine abnormalities, and gastrointestinal disorders at greater prevalence than typically developing children. They also experience subclinical electrical discharges at prevalence as high as 61% and 100% in studies using long term monitoring (Frye & Rossignol, 2016).

While many of these comorbidities can worsen the symptoms of an autism spectrum disorder and anxiety, sleep disorders and gastrointestinal disorders play noteworthy roles in overall quality of life as they contribute to the experience of anxiety among children who have an autism spectrum disorder. Anxiety is a stand-alone diagnosis, but it is also a symptom of many conditions, including ASD, sleep disturbances, and gastrointestinal disorders, creating a level of uncertainty surrounding the actual cause of anxiety among children with an autism spectrum disorder (Shelby et al., 2013).

Sleep Disturbances

Children with ASD experience a wide range of sleep disorders, including prolonged sleep onset latency, frequent nighttime awakenings, reduced sleep duration, and daytime sleepiness (Frye & Rossignol, 2016). Over half of children with ASD
have at least one sleep disorder, with some estimates as high as 86% of ASD children experiencing a sleep disorder each day (Klukowski, 2015). The most common complaints from children with ASD are related to insomnia and secondary insomnia.

Children respond to sleep disturbances differently than adults. Sleep disturbances impact overall behavior during the day and can result in poor executive functioning, impaired social interaction, and anxiety. Sleep disturbances have been found to produce increased anxiety scores for children with ASD using both parent- and clinician reported measurement instruments (Nadeau et al., 2015). Similarly, in a study evaluating predictors of sleep quality among children who have an autism spectrum disorder, anxiety was found to be the strongest predictor, as compared to developmental regression, ASD subtype, sensory sensitivity, gastrointestinal disorders, and age (Hollway et al., 2013).

**Gastrointestinal Disorders**

Gastrointestinal symptoms impact up to 91% of children with ASD (Frye & Rossignol, 2016). These conditions range from chronic constipation or diarrhea to abdominal pain to dysbiosis of the enteric microbiome (McElhanon et al., 2014). Many of these gastrointestinal disorders share genetic and environmental risk factors with ASD, and recent research indicates that these gastrointestinal symptoms may contribute in some way to the overall severity of the symptoms of ASD, including anxiety (Hsiao, 2014).
Children who experience GI problems have significantly higher prevalence of anxiety (Mazurek et al., 2013). The relationship between gastrointestinal health and anxiety is not limited to individuals with an autism spectrum disorder. Children with functional abdominal pain experience anxiety with greater prevalence than is experienced by children who do not have functional abdominal pain (Shelby et al., 2013). The lifetime odds ratio for an anxiety disorder is 4.9 for children who have functional abdominal pain as compared to children who do not have functional abdominal pain.

**Causes of Autism Spectrum Disorders**

There is no single cause of autism spectrum disorders. Many risk factors have been identified and numerous positive relationships between the onset of autism spectrum disorders and a wide range of genetic and environmental factors have been identified. Existing research indicates that autism spectrum disorders are caused by a complex interaction between these genetic and epigenetic predispositions and environmental factors.

**Pre- and Perinatal Factors and Autism Spectrum Disorders**

In a Swedish cohort study, researchers identified relationships between maternal body mass and ASD in offspring (Gardner et al., 2015). Both maternal and paternal obesity were found to produce a significant odds ratio above 1.0 compared to
healthy weight parents in population-level data. These odds ratios fell within the range of 1.0 when matched with siblings, indicating that obesity may not be a risk factor but rather a proxy marker of ASD risk.

The same researchers found that extremes in overall weight gain during pregnancy, both large and small amounts of gestational weight gain, produced increased odds ratios that persisted not only through population level analyses but also when matched with siblings (Gardner et al., 2015).

Australian researchers have also identified relationships associated with an ASD diagnosis in a case-control study (Glasson et al., 2004). This study identified relationships between threatened pregnancy loss, epidural usage, induction of labor, planned or emergency cesarean birth, fetal distress, and low APGAR scores after birth as having relationships with cases in the study. Many of these factors are related, as induction of labor is known to increase the risk of emergency cesarean, fetal distress, and low APGAR scores after birth (Caughey et al., 2014). The relationship between these factors and the onset of autism spectrum disorders is not well understood.

**Genetics and Epigenetics**

One of the strongest influences in the development of an autism spectrum disorder is a genetic predisposition. In studies evaluating incidence among twins, siblings, families, and overall populations, clear genetic links have been established with multiple associated genes (Yoo, 2015). A total of 61 different genes have been
found to be associated with autism spectrum disorders (Yuen et al., 2017). Genes, however, are not able to fully explain the modern surge in ASD prevalence.

Genes intersect with the field of environmental health through the field of epigenetics, which refers to the way in which environmental factors influence genetic expression over multiple generations. Epigenetic influences alter gene expression, a phenomenon which is distinct from genetic mutations or alterations in the actual genetic code. Because both environmental factors and genetic factors are associated with ASD, neither model fully explains the cause of ASD or the rapid increase in prevalence observed over the last several decades.

Epigenetic expression alterations influence future generations long after the original exposure (Kubota & Mochizuki, 2016). For example, postnatal mental stress can alter DNA methylation in the mother and her male children up to the third generation. Environmental factors which are known to influence genetic expression include perinatal BPA (bisphenol A) exposure, maternal stress during pregnancy, PCB (polychlorinated biphenyls) exposure, and household lead exposure (Keil & Lein, 2016).

**Hygiene Hypothesis**

A final emerging hypothesis for the prevalence of autism spectrum disorders is known as the hygiene hypothesis or the “old friends” hypothesis, and is related to the sanitation-related public health advancements achieved in the early 1900s.
According to the hygiene hypothesis, children require frequent exposure to beneficial microbes during early development to establish a robust and healthy immune system. In the absence of that exposure, children are at increased risk for an assortment of chronic conditions including asthma, allergies, autism spectrum disorders, and inflammatory disorders (Becker 2007).

The Hygiene Hypothesis is also used to explain increases in prevalence of chronic gastrointestinal disorders, which are also experienced more frequently by children with ASD as compared to typically developing children (Rook et al., 2013). The gastrointestinal track is home to millions of microbes which play a beneficial role in immune function, metabolic health, and in brain and behavioral development (Rook et al., 2013).

As many beneficial neurotransmitters are produced in the gut, and healthy bacteria contribute to the development of these neurotransmitters, the overall presence of healthy bacteria in the gut has been linked to multiple conditions related to brain development (Rook et al., 2013). When rural and urban populations are compared, this early exposure to beneficial bacteria has been found to stimulate healthy immune function which is necessary for normal brain development (Becker, 2007). While the relationship between beneficial bacterial exposure and healthy brain development is clearly established, the relationship is not yet clearly understood. Researchers are still exploring the direction of this relationship and its overall contribution to the development of conditions such as ASD.
Treatments for Autism Spectrum Disorders

Just as there is no single cause of autism spectrum disorders, there is no single cure for autism spectrum disorders. ASD is a complex spectrum of disorders which impacts individuals in different and unique ways. Existing treatment goals focus on addressing the most pressing symptoms and improving overall quality of life for individuals who live with an autism spectrum disorder.

The most pressing needs identified are those related to quality of life, such as social support, anxiety and stress relief, and emotional regulation (White et al., 2016). ASD students’ needs are often misunderstood by teachers, and students demonstrate a need for increased self-efficacy and self-advocacy (White et al., 2016). Because anxiety is a symptom which permeates the social experiences of those with an ASD, solutions which can address the underlying anxiety hold potential to improve self-efficacy and self-advocacy.

The need to address anxiety among children with an autism spectrum disorder is one need recognized by both teachers and students alike (Ashburner et al., 2010). When surveyed, teachers identified anxiety as being the biggest treatment need experienced by students with an autism spectrum disorder, with other priority needs including oppositional behavior, social problems, adaptation related issues, and perfectionism (Ashburner et al., 2010). Each of these other factors are indirectly
related to the underlying concern of anxiety among children with an autism spectrum disorder.

**Integrative Medicine for Autism Spectrum Disorders**

Despite these needs being widely recognized and understood, providers have little to offer as a solution. Providers report knowledge gaps related to the resources, needs, and available treatment options for children with ASD, and both providers and parents report communication gaps in treatment-related decisions (Levy et al., 2016).

Due to the lack of resources available in conventional medicine to address these needs, many parents are opting to rely on CAM (Complimentary and Alternative Medicine) treatments to address the symptoms of an autism spectrum disorder (Owen-Smith et al., 2015). There is a wide range of treatments available in the CAM classification, with efficacy varying by treatment. Treatments frequently chosen by parents of children with an autism spectrum disorder include special diets, dietary supplements, herbs and essential oils, and vitamins such as B12 injections.

In surveys, over 50% of parents of children with an autism spectrum disorder report using some sort of CAM treatment with their child, with some surveys revealing that as many as 88% of parents have used CAM at some point in their child’s treatment (Levy et al., 2016; Owen-Smith et al., 2015). Predictors of CAM use include higher parental educational status, younger age of the child with an ASD, and
the lack of success with previous attempts at addressing symptoms with prescription drugs (Owen-Smith et al., 2015).

**Conclusion**

Children with an autism spectrum disorder experience higher prevalence of anxiety than children who do not have an autism spectrum disorder (Kerns et al., 2014). This burden impacts society as a whole, as well as children and their families individually (Buescher et al., 2014). While the cause of ASD is not well understood, many environmental and genetic factors have been identified as potential causal factors (Kubota & Mochizuki, 2016). Treatments for anxiety among children with an autism spectrum disorder are lacking, causing parents to turn to alternative solutions in the hopes of achieving some improvement in overall quality of life (Owen-Smith et al., 2015). The safety and efficacy of many CAM treatments for children with an autism spectrum disorder is not well established. There is a growing need for non-invasive solutions to the anxiety experienced by children with an autism spectrum disorder that are both safe and effective.

**The Current Study**

The purpose of this study is to measure the effect of a non-invasive essential oil-based aromatic intervention on both subjective and objective anxiety scores among children ages 6-11 who have an autism spectrum disorder.
**Research Question 1:** What effect does the environmental scent in medical office patient examining rooms have on anxiety among children with an autism spectrum disorder during routine office visits as measured by the STAI-CH state anxiety inventory?

**Hypothesis 1:** When controlling for age, sex, and the presence of an anxiety diagnosis, children with an autism spectrum disorder who inhale bergamot essential oil during their medical appointments will have lower scores on the state anxiety scale than children who do not inhale bergamot essential oil.

**Research Question 2:** What effect does the environmental scent in medical office patient examining rooms have on anxiety among children with an autism spectrum disorder during routine office visits as measured by blood pressure?

**Hypothesis 2:** When controlling for age, sex, and the presence of an anxiety diagnosis, children with an autism spectrum disorder who inhale bergamot essential oil during their medical appointments will have lower blood pressure readings than children who do not inhale bergamot essential oil.

**Research Question 3:** What effect does the environmental scent in medical office patient examining rooms have on anxiety among children with an autism spectrum disorder during routine office visits as measured by heart rate?
**Hypothesis 3:** When controlling for age, sex, and the presence of an anxiety diagnosis, children with an autism spectrum disorder who inhale bergamot essential oil during their medical appointments will have a lower heart rate than children who do not inhale bergamot essential oil.
CHAPTER 2: LITERATURE REVIEW

Introduction

Treating an autism spectrum disorder is a complex, multi-discipline task, as the lack of a single causal factor reduces opportunities for a single cure or treatment modality. Many treatments are aimed at improving overall quality of life for individuals with ASD by addressing various symptoms, with varying degrees of efficacy. Due to the heterogeneity of ASD symptoms, including diversity in phenotype, genetic factors, and outcomes, cases of autism spectrum disorders are treated with a combination of treatments, each of which addresses a different symptom or set of symptoms (Masi et al., 2017). This combination is often unique to the individual, based upon the symptoms he or she experiences.

Treatments are diverse and reflect a range of interventions, including dietary approaches, behavioral therapy, dietary supplements, pharmaceuticals, and holistic or CAM medicine (Vasa et al., 2014). Because anxiety is one of the most common symptoms and comorbidities of ASD, many treatments are designed to address this symptom specifically. Authors of some studies use the term *anxiety* as a general symptom, while others specify a specific anxiety diagnosis (Vasa et al., 2014). This review focuses on treatments for autism spectrum disorders that specifically address anxiety as both a symptom and a comorbidity, and the theories which are useful for future studies of treatments of anxiety among children who have an autism spectrum disorder.
Two underlying problems persist across treatments for anxiety among children who have an autism spectrum disorder. These include a lack of efficacy, and high incidence of adverse events (Vasa et al., 2014). Noninvasive solutions for anxiety have frequently been found to be ineffective, while stronger pharmaceutical interventions often produce a high incidence of adverse events, while also failing to achieve efficacy.

This review identifies current treatments which are used to address anxiety among children who have an autism spectrum disorder, both noninvasive and pharmaceutical, identifies unmet needs which persist among this population, and suggests potential solutions to this problem.

**Dietary Interventions**

Dietary interventions to address anxiety among children who have an autism spectrum disorder are popular among the general autistic population, perhaps due to the perceived lack of invasiveness associated with the treatment option. Between 15% and 38% of children with an autism spectrum disorder have used dietary interventions (Perrin et al., 2012). The most popular dietary approach to autism spectrum disorders is the gluten free and casein free diet. Gluten is the protein matrix found in wheat, and less commonly in barley and rye, and casein is the protein found in dairy products.

According to the theory of the gluten free and casein free (GFCF) diet, children with autism spectrum disorders are unable to fully digest these proteins,
leaving protein fragments or peptides to circulate the body. These peptides are believed to ultimately bind to opioid receptors, where they can influence brain chemistry, ultimately influencing behavior (Hyman et al., 2015).

The GFCF approach restricts the child’s diet by eliminating many grains and dairy products, which are key sources of nutrients vital to the healthy growth and development of a child. Children on this diet must strictly avoid all wheat, barley, and rye, along with some oats, and all dairy products, including cheese, milk, and butter.

Despite its popularity, the diet has produced mixed results in the few studies which have evaluated its efficacy. In an open label study conducted among 80 children who have an autism spectrum disorder in Iran, the diet was found to produce a statistically significant change in autistic symptoms, including anxiety, as well as significant improvements in overall gut health among the participants, as evidenced by a reduction in gastrointestinal symptoms. While the effect size was large for changes in gut health, the total effect of reduction in autistic symptoms was minimal (Ghalichi et al., 2016).

This is in contrast to the results of a 2015 study of 14 children who received the GFCF diet in a double blinded trial in New York. This study also evaluated overall autistic symptoms, including anxiety, as well as gastrointestinal symptoms on multiple scales. There was no change from baseline to follow-up in any of the outcomes measured (Hyman et al., 2015).
Another diet utilized in autism spectrum disorder treatment is the ketogenic diet. This diet is distinguished by an extremely high intake of fat, minimally sufficient intake of protein, and insufficient intake of carbohydrates, forcing the body to burn fat for fuel rather than carbohydrates (El-Rashidy et al., 2017). In this diet, children receive approximately 10% of their overall caloric intake from carbohydrates, which is approximately 8-10 grams a day.

When compared to the GFCF diet and a control group, the ketogenic diet produced significant improvements in overall autism spectrum disorder symptoms, including anxiety, although outcomes such as behavioral symptoms were better treated with the GFCF diet (El-Rashidy et al., 2017). The limitations of treating autism spectrum disorders and anxiety through dietary interventions include the requirement for strict adherence to the diet, resulting in poor patient compliance, and the lack of evidence that such dramatic alterations to the child’s diet produce practically significant effects. Additionally, the long-term risks of adopting a strict and potentially nutrient deficient diet are not known.

**Cognitive Behavioral Therapy**

Behavioral interventions provide well established treatments for autistic symptoms in general, and anxiety specifically. Cognitive Behavioral Therapy (CBT), which involves professional counseling for 60-90 minute sessions with a licensed therapist over the course of sixteen weeks, has been found to be highly effective at
reducing anxiety among children who have an autism spectrum disorder when compared to control groups and waitlisted groups of children who have an autism spectrum disorder (Storch et al., 2015; White et al., 2013; Wood et al., 2015).

The effect of CBT on children who have an autism spectrum disorder is large, with one study finding that 79% of children in the CBT group achieved positive responses to treatment while only 28.6% of children on the waitlist had positive responses (Wood et al., 2015). Another study found that 68.8% of children in the CBT treatment group responded to treatment as compared to 37.5% in the control group (Storch et al., 2015).

Efficacy has been found when the outcome measured is both generalized anxiety and more specific social disabilities due to anxiety (White et al., 2013). When CBT-like interventions designed to target the social effects of anxiety on children who have an autism spectrum disorder are utilized, overall social functioning improves.

This approach to anxiety management is beneficial because it can be combined with other treatments, however because CBT is a multi-modal therapy with interventions that are clinic based, school based, and peer based, the weekly maintenance requirements and overall cost can be prohibitive for many families. While the intervention has shown to be effective a month after the conclusion of the treatment, long-term studies are needed to identify efficacy many months or years after the initial 16 week treatment has concluded (Storch et al., 2015).
As a result of the complexity of CBT, CBT-inspired programs have been developed to achieve the same benefits without the barriers to care. One example of this approach is the Coping Cat program, a 16 week program that was designed to reduce some of the barriers of traditional CBT delivery requirements (McNally Keehn et al., 2013). At the end of this treatment program, 58% of children with an autism spectrum disorder no longer qualified for an anxiety diagnosis, while 100% of the children in the waitlisted group continued to meet the criteria for an anxiety diagnosis.

**Media-Based Interventions**

Other attempts at addressing the barriers to care that exist with CBT include utilizing media-based interventions which feature the core components of CBT in more user-friendly methods. One such intervention is a video game, MindLight, that can be played on a handheld device which uses the most validated component of CBT, exposure to threatening cues (Wijnhoven et al., 2015). Mindlight integrates biofeedback so that children can achieve higher levels in the game by addressing threatening cues and overcoming anxiety.

Similar approaches are utilized in medical offices. In a dental clinic associated with Boston Children’s Hospital, a video-based intervention which featured peer modeling of children undergoing preventive dental care was shown to children who have an autism spectrum disorder to address anxiety faced in the medical setting.
(Isong et al., 2014). This intervention has also been shown to be effective, and children who have an autism spectrum disorder achieve greater reduction in overall anxiety if the videos are watched more than once.

Handheld devices, such as the iPad, can also be used to deliver social scripts that can be used by children who have an autism spectrum disorder to overcome social anxiety. Because lack of preparedness contributes to higher anxiety among children who have an autism spectrum disorder who are exposed to new settings or changes in settings, scripts can serve as a preparedness tool which empowers them to clearly communicate their needs and concerns. Social scripts are based on social stories, which are step-by-step tools used to empower children to face uncertainty (Johnson et al., 2014).

Other Therapy-Based Interventions

In addition to CBT and media-based interventions, group therapy and music therapy have been found to be effective tools for reducing overall anxiety among children with an autism spectrum disorder (McConachie et al., 2014; Porter et al., 2016). While group therapy has been found to produce effect sizes comparable to those produced by studies evaluating CBT, music therapy produces minimal benefits to children who have an autism spectrum disorder when anxiety is the outcome of interest.
**Dietary Supplements**

Vitamin and mineral supplements are also used frequently with children on the autism spectrum, with varying results. While it has been found that the nutrient intake of an autistic child is quite similar to a child without an autism spectrum disorder, both groups of children have intake of key nutrients that fall below the recommended daily levels (Hyman et al., 2012).

When children who have an autism spectrum disorder consume a multi-vitamin and mineral supplement, not only does nutritional status improve, markers such as oxidative stress and methylation are also improved (Adams et al., 2011). While multivitamin supplementation does not directly reduce anxiety among children who have an autism spectrum disorder, improvements in core bodily functions may play a role in improving overall adaptation to stress in the environment.

Specific nutrients have also been evaluated for use with symptoms of autism spectrum disorders. These range from large doses of single vitamins to dietary supplements such as fish oil and probiotics (Santocchi et al., 2016). Outcomes vary depending on the specific nutrient, the overall duration, and the outcomes being measured.

Folic acid has been found to significantly reduce the symptoms of autism spectrum disorders, particularly those symptoms associated with anxiety and social behaviors when used as a dietary supplement which delivers the recommended daily allowance of the nutrient over a span of three months (Sun et al., 2016). Social
awareness and motivation has also improved after daily intake of omega-3 fatty acid supplements over a period of 3 months (Ooi et al., 2015).

Specially formulated supplements are also used in some situations. An anti-inflammatory flavonoid which consists of luteolin, quercetin, and rutin has been studied in a 26-week trial with behavioral changes as a key outcome (Taliou et al., 2013). In this trial, the supplement produced a transient phase of irritability during the first 1-6 weeks for half of the participants, but produced significant improvements in overall behavior and maturity.

Not all popular supplements have been found to reduce symptoms of anxiety. Dietary enzymes which target proteins such as gluten and casein are used as supplements to, or alternatives to, the GFCF diet. Compared with placebo, these supplements have not been found to produce any statistically significant changes in outcomes such as anxiety, sleep quality, or behavior (Munasinghe et al., 2010).

While dietary supplements are generally regarded as safe and potentially beneficial interventions due to low levels of adverse effects found in research studies, potential efficacy varies dramatically across treatment protocols (Gogou & Kolois, 2017).

**Herbal Supplements**

Few herbal supplements have been evaluated for efficacy with children who have an autism spectrum disorder. Reviews of complementary and alternative
medicine (CAM) with children who have an autism spectrum disorder identify dietary supplements, complementary therapies, massage, and the herbal supplement *Panax ginseng* as effective tools for use in a comprehensive protocol (Lofthouse et al., 2012; Bang et al., 2017).

Ginseng is an herbal supplement which is ingested in a tablet form. A case series of three patients who consumed ginseng for a 4-week period found modest improvements in social behaviors among children who have an autism spectrum disorder, but did not produce significant changes in overall anxiety scores or related symptoms (Niederhofer, 2009).

**Pharmaceuticals**

While dietary interventions and vitamins offer noninvasive treatments, many pharmaceuticals are also used to address anxiety among children who have an autism spectrum disorder. Psychopharmacological treatments used to address symptoms of autism spectrum disorders include risperidone, a second generation antipsychotic approved by the FDA for autism spectrum disorder-related irritability, aripiprazole, another FDA-approved psychotropic drug for irritability in children, and various selective serotonin re-uptake inhibitor (SSRI), and anxiolytics (LeClerc & Easley, 2015; Vasa et al., 2014).

Efficacy varies depending on the drug utilized and the treatment group’s characteristics. Among psychopharmacological treatments for anxiety, efficacy ranges
from no effect up to 66% of children demonstrating improvement (Vasa et al., 2014). These outcomes are not as strong as the outcomes produced by less invasive CBT and similar therapeutic programs. Additionally, existing studies evaluating efficacy and safety of these drugs among the autistic community are small and often fail to include a control or placebo group (Vasa et al., 2014).

Not only is the strength of evidence poor, safety of the use of powerful pharmaceuticals with children who have an autism spectrum disorder is questionable. The prevalence of adverse events among children with autism spectrum disorders who are taking pharmaceuticals for symptomatic relief is high, with many patients and study participants discontinuing treatment as a result of the side effects (Vasa et al., 2014; LeClerc & Easley, 2015).

**Utilization of Treatment**

While the treatment of autism spectrum disorders varies by child and is based upon the unique symptoms and characteristics experienced, there are some age-related trends and norms. For noninvasive treatments such as school based interventions, private therapy, and dietary changes, utilization is highest during the preschool years of ages 2-5 and the early elementary ages of 6-11 (Mire et al., 2015). Pharmaceutical treatments such as mood stabilizers, antidepressants, and anxiolytics are higher among adolescents ages 13-17.
One element of the change in treatment strategy is the variation in efficacy due to age at treatment. Interventions such as speech therapy and non-pharmacologic options have been found to be more effective when utilized early in childhood as early intervention leads to improved outcomes (Pellecchia et al., 2016). Children with higher levels of social anxiety and increased age are less likely to benefit from noninvasive interventions.

**Treatment Efficacy**

Treatment efficacy of the existing myriad of options available to address symptoms of anxiety among children who have an autism spectrum disorder remains low. Many therapies, drugs, and supplements are used, often in combination, but fail to adequately resolve symptoms such as anxiety which effect overall quality of life (Dawson, 2017; Coury, 2011).

Many of the studies evaluating efficacy are underpowered and fail to fully categorize the populations being evaluated (Weitlauf et al., 2017). Additional studies investigating the effects of both existing and novel solutions to anxiety and other autistic symptoms are urgently needed, due to the rapid increase in prevalence of ASD.

Further complicating the treatment dilemma is the contribution of the large placebo effect on children who have an autism spectrum disorder. This placebo effect influences both the patient perspective and the parental response. In a survey of
parental responses to the efficacy of treatments, parents were likely to report improvement that was classified as “somewhat” and “dramatic,” for most interventions attempted, and their definition of efficacy was not clearly defined (Goin-Kochel et al., 2009).

**Parental Stress and Anxiety**

Parents of children with an autism spectrum disorder identify additional barriers to care for children who require solutions faster than this rapidly-growing field of research can provide evidence regarding the safety and efficacy of these solutions. One barrier to care is the time delay between parental concerns about child development and provider response which leads to diagnosis (Zuckerman et al., 2015). When parents have concerns about their child’s development, they are more likely to receive a passive response indicating that the child will outgrow the concern or that their behavior is normal, than to receive an active response which includes screening for developmental delays and referrals for a diagnosis.

When a passive response is received, there is a 2.5-3 year time delay between the age in which the parents first bring concerns about their child’s development to the care provider and then the diagnosis is actually achieved. These events occur, on average, at 2.3 years and 5.2 years, respectively. Due to the requirements for early intervention to boost efficacy, critical time is lost during this delay (Zuckerman et al., 2015).
These frustrations are further complicated by the stress produced by being not only the child’s primary advocate but also the child’s primary caregiver. Parents of children with an autism spectrum disorder experience greater amounts of stress than parents of typically developing children (Estes et al., 2009). Parents are more likely to experience stress and anxiety from caregiving demands when social and economic support are poor, when perceived limit setting ability is low, and when the ASD symptom severity is high (Falk et al., 2014).

The stress of caring for children with an autism spectrum disorder and any related intellectual or developmental disabilities produces a secondary need for treatment of the family unit to provide care for the caregiver. These interventions are similar to some of the mindfulness and anxiety reducing strategies which offer supportive care for similar symptoms experienced by children with an autism spectrum disorder (O Donnchadha, 2017).

Parental anxiety is not a standalone concern. Overall levels of parental anxiety influence efficacy for treatments of anxiety among children who have an autism spectrum disorder (Reaven et al., 2015). The relationship is bidirectional and reciprocal, and interventions which break the cycle of anxiety in the family unit have a ripple effect, improving the quality of life for others in the home.
**Parental Response**

Parents of children with an autism spectrum disorder and anxiety report frustration with the lack of safe and effective treatment options (Levy et al., 2016). In a qualitative research study among parents and care providers of children who have an autism spectrum disorder, participants disclosed that their providers suffer from knowledge gaps regarding the existing treatment options and associated efficacy, that more communication about choices in treatment was needed, and that CAM and integrative interventions created conflict in the patient-provider relationship (Levy et al., 2016).

As a result, parents report self-treating their children with CAM and related interventions, and over half of the parents interviewed reported using CAM without assistance or guidance from their care providers. In another sample, 88% of parent participants reported using CAM for their children who have an autism spectrum disorder and another sample found that 100% of parents surveyed used CAM to treat autism spectrum disorders (Owen-Smith et al., 2015; Huang et al., 2013). Parents who chose to use CAM treatments for their children tend to be highly educated with children who were preschool and early elementary ages.

Not all physicians oppose CAM treatments for children with an autism spectrum disorder and physicians report similar frustrations with the lack of treatment options and available evidence (Golnik & Ireland, 2009). When surveyed, physicians
who promote CAM with their patients were more likely to desire additional training and education in the use of CAM.

Integrative Medicine

Because parental acceptance of CAM is high and physicians are lacking in available treatment options for children who have an autism spectrum disorder which are both safe and effective, parents are increasingly interested in research and associated treatment options for their children which involve both conventional and alternative solutions (Huang et al., 2013). The use of CAM in childhood is a growing field with high prevalence among all children, including those who do not have an ASD (Lucas et al., 2015). The challenges that are posed by the increased utilization of CAM with children include lack of available research on safety and efficacy, inconsistent training standards for educational preparedness, and lack of communication between providers and parents regarding CAM usage (Lucas et al., 2015).

Within the autistic population, the need for early intervention often overrides the need for additional research in the field, as parents have stated a preference to try something that may work while early intervention is still possible, rather than wait for research that may take years or even decades to provide conclusive evidence (Levy et al., 2016). Integrative approaches to anxiety among children who have an autism spectrum disorder that are considered to be safe and potentially useful include dietary
Supplements, dietary interventions, and hydrotherapy, while other interventions, such as chelation therapy, hyperbaric oxygen chambers, and secretin treatment are considered unsafe due to documented adverse outcomes (Klein & Kemper, 2015).

**Aromatherapy, ASD, and Anxiety**

Aromatherapy is another CAM related therapy that poses minimal risk and has the potential to offer noninvasive treatment for ASD symptoms such as anxiety. Aromatherapy is a component of integrative health which utilizes the expressed or distilled volatile extracts of a plant, which are liquids and lipid-soluble. These plant volatile oils are commonly known as essential oils. Essential oils can be extracted from many different plants and the potency and chemical composition of the oil varies depending on the specific species of plant and the plant’s growing conditions.

Essential oils are typically extracted from crude plant matter through steam distillation. This process extracts only the low molecular weight aromatic components of the plant, which are used medicinally in many parts of the world. Essential oils from citrus plants may also be extracted through cold pressing. Because citrus plants contain large amounts of essential oil, the product can be obtained by pressing the peels of the fruit which are often discarded after production of various food products. This enables citrus oils to contain certain molecules which would otherwise be too heavy to be extracted through steam distillation.
While the most common uses of aromatherapy include the development of personal care products and air freshening diffusion throughout a room, the medicinal approach to aromatherapy utilizes a higher dose of inhalation, higher doses of topical application, and essential oil ingestion to achieve specific health benefits. Clinical studies evaluating efficacy produce varying results depending on the specific essential oil, the administration method, and the condition being treated.

**Aromatherapy for Anxiety**

Knowledge about the effects of aromatherapy on anxiety among children who have an autism spectrum disorder is limited. One study evaluates the use of aromatherapy for sleep quality in children who have an autism spectrum disorder specifically. In 2006, twelve teenage children with an autism spectrum disorder received aromatherapy massages, using a traditional massage technique and lavender essential oil, for three nights. Sleep quality was contrasted with 14 nights without the aromatic massage. Children were evaluated visually every 30 minutes through the night and outcomes included sleep onset and duration. This study did not find any beneficial effects of the lavender oil and massage combination (Williams, 2006). While other studies have been announced through press releases as being in-progress, no other published clinical trials have evaluated the safety and efficacy of essential oil inhalation on children with an autism spectrum disorder.
Aromatherapy is used to treat anxiety in other populations successfully through a variety of methods. Inhalation of the essential oils results in exposure of the substance to the limbic system of the brain, which plays a role in learning and memory. While traditional aromatherapeutic use for anxiety reduction involves a wide range of oils, the oils supported by clinical literature include bergamot (*Citrus bergamia*), lavender (*Lavendula angustifolia*), and rosemary (*Rosmarinus officinalis*) (Hosseini et al., 2016; McCaffrey et al., 2009; Chang & Shen, 2011). Of these oils, bergamot appears to provide the most effective results.

**Bergamot Oil for Anxiety**

*Citrus bergamia* is a small, round fruit typically grown in a small region of southern Italy. The peels are used to produce an essential oil through cold expression. The effects of bergamot oil for anxiety have been documented in the literature, but not specifically on children who have an autism spectrum disorder (Chang & Shen, 2011; Ndao et al., 2012; Ni et al., 2013).

In a medical setting specifically, researchers evaluated the use of bergamot essential oil in the environment for otherwise healthy children prior to stem cell transplants to reduce anxiety. In this study, anxiety was measured by using the State-Trait Anxiety Inventory for children (STAI-CH) upon arrival and after the exposure and found that healthy children who were exposed to the aroma were less anxious.
about the procedure than children exposed to usual hospital environmental smells (Ndao et al., 2012).

This effect is also found in adults. The STAI (adult version) has been used to evaluate the effect of bergamot aroma on anxiety in adults awaiting surgery as compared to the usual medical office smells, and patients who were exposed to bergamot essential oil were found to experience less anxiety about the event than those exposed to the usual scents (Ni et al., 2013).

Similarly, the oil has been found to reduce overall stress with autonomic nervous system regulation after being inhaled by elementary school teachers, with heart rate and blood pressure as outcome markers (Chang & Shen, 2011). The oil has also been found to improve parasympathetic nervous system activity with a reduction in salivary cortisol levels in adult females who were exposed to the oil via inhalation (Watanabe et al., 2015). In this study, the oil improved anxiety scores using the STAI adult version as well as through saliva samples.

**Bergamot Oil Suitability**

Bergamot oil has a mild, citrus-like aroma which is due to the large concentration of the chemical limonene, which comprises 25-53% of the oil’s total composition (Navarra et al., 2015). Limonene is also found in orange, lemon, and lime peels. The oil is also rich in linalool (2-20%) and linalyl acetate (15-40%), which are the active components of lavender essential oil (Navarra et al., 2015).
Unlike other essential oils, which are steam distilled, bergamot is typically cold pressed from the peels and may also contain nonvolatile components, including bergapten, which is present at approximately 0.2%.

In addition to its anxiolytic effects, bergamot oil is known to have anti-inflammatory benefits, mild antimicrobial activity, and mild analgesic effects (Navarra et al., 2015). Widespread use is also found in the food industry as the peels of the bergamot fruit are used as the flavoring in earl grey tea. Bergamot oil is generally considered to be quite safe with rare adverse effects reported. These are due to the bergapten component, which is known to be phototoxic when applied to the skin in large amounts (Navarra et al., 2015).

In rat models, bergamot oil has been found to reduce markers of anxiety through inhalation with effects similar to the pharmaceutical diazepam (Saiyudthong & Marsden, 2011). The gentle aroma and large range of safety combined with the effects documented in the literature make bergamot an ideal candidate for evaluation as a gentle yet effective treatment for anxiety among children who have an autism spectrum disorder.

**Theoretical Basis**

The theoretical basis for this study is derived from the Transactional Model of Stress and Coping, developed by Lazarus and Folkman in 1984. This model provides framework which describes the process of analyzing and coping with stressful events.
The process involves two appraisal constructs, collectively referred to as cognitive appraisal, followed by two coping constructs, and it is based upon the concept that stressful experiences consist of transactions between the person and environment (Glanz et al., 2008).

The first appraisal is the primary appraisal, which occurs when the individual who is faced with a stressor evaluates the significance of the threat. During this stage, the individual uses both cognition and emotion to determine whether or not the threat is changeable, controllable, positive, or irrelevant (Lazarus and Folkman, 1987). He or she determines whether or not the stressor is significant and meaningful using perceived susceptibility and perceived severity (Glanz et al., 2008).

During the secondary appraisal stage, the individual evaluates the controllability of the stressor within the context of the resources available for coping. This construct is related to self-efficacy as it evaluates the psychological, social, and cultural resources which may be available to face the challenge (Glanz et al., 2008). Elements of the situation which are appraised in this stage include perceived controllability of the situation (ability to change), perceived control over emotions, and perceived efficacy of coping resources.

Because both appraisals consist of perceived threats and perceived resources, it is applicable to situations and individuals which involve both actual threats and perceived threats. Interventions consist of both addressing a real threat that may exist and addressing the perceptions about the situation in terms of both the significance of
the threat and the presence of resources that enable an individual to cope with the threat or stressor.

Coping constructs consist of the actual strategies used to address these appraisals. These include problem-focused coping and emotion-focused coping or emotional regulation (Cohen and Axelrod, 1984). Problem-focused coping involves information seeking and actually altering or managing the situation (Glanz et al., 2008). Emotional regulation involves addressing the intra- and interpersonal factors which influence perceptions related to the stressor. These consist of targeting the perceptions about the stimuli, positive events, optimism, seeking social support, and other interventions which empower the individual to manage their emotional response to the stressor (Glanz et al., 2008).

Treatment involves multiple approaches, including altering the environment to make the stressors more relaxing and less threatening. For children who have an autism spectrum disorder and experience medical visits as a stressor, environmental changes such as pleasant aromas, adjustments to the lighting, or changes in the sounds are effective tools that can be used to reduce anxiety as problem-focused coping interventions on a large scale and as emotional regulation tools available to an individual on the personal level.
Transactional Model of Stress and Coping Research Applications

This model has been used in a wide range of settings where the underlying similarity is an intervention which is designed to influence stressors faced by specific subsets of the population. It served as the theoretical basis for an intervention to identify women at risk of depression during the third trimester based upon their perception of neighborhood environment, social support, and avoidance coping for African American women in Chicago (Ciurgescu et al., 2015).

The model was also used to identify factors that can strengthen coping skills for women who have chronic illness and are transitioning out of prison. It utilized strategies such as motivational interviewing to address constructs of the model and provide tools that can be used to reduce stress and anxiety (Colbert & Durand, 2016). The model was also used to boost care retention for individuals with HIV by identifying interventions and practices on both the intra- and interpersonal levels related to stress and coping (Graham, 2015).

The model is an effective tool across a diverse range of populations, with the underlying similarity being the need for interventions that boost coping skills for stressful and anxiety producing environments. Whether the situation involves an adult woman transitioning to life outside of prison or an autistic child facing the stress of a medical care appointment, the model of stress and coping serves as a useful tool for directing interventions.
Suitability of the Model for Anxiety and ASD

The experience of anxiety for a patient in a medical setting is influenced by many factors represented in the Transactional Model of Stress and Coping. Familiarity, friendliness of the provider, environmental exposures in the waiting and exam rooms, and other factors may be related to the overall appraisal a child experiences when visiting a provider.

If it is found that the presence of a bergamot aroma in the examining room at a care provider’s office reduces the overall experience of a child at a medical visit, this intervention can influence the perception of a child by addressing both primary and secondary appraisals.

The primary appraisal utilizes a cognitive approach which emphasizes past experiences with the stressor. Previous encounters at a provider’s office influence how the child perceives the visit and whether they will experience a routine medical check-up as a threat or as a manageable experience.

By intervening at a medical visit, the alteration in environmental aroma can enable the patient to develop positive experiences which will alter perception of risk in future encounters. The alteration in aroma can also influence secondary appraisal as well, by providing the child with a resource that can be used to cope with the stressor.
Conclusion

Many challenges exist which hinder the totality of care for children on the autism spectrum as it relates to the symptom of anxiety. These include lack of documented efficacy, high incidence of adverse effects, total time to diagnosis, and parental stress. Routine requirements, such as medical office visits, add increased stress to the entire family unit.

Many dietary changes, holistic interventions, and environmental changes have been found to be effective solutions for typically developed children, but it cannot be assumed that these interventions are also effective for children who have an autism spectrum disorder. Children who have an autism spectrum disorder are often either hypo- or hypersensitive to sensory stimuli such as changes in sight, sound, smell, and texture (Ashwin et al., 2014).

This study seeks to evaluate the role of a sensory enhanced environment through the use of bergamot essential oil as a tool to improve both problem-focused coping and emotional regulation of children with an autism spectrum disorder who require routine medical visits. Sensory adapted medical offices have been found to be useful tools that improve overall quality of care among children with an autism spectrum disorder in the dental environment. In a 2015 study, researchers found that children who have an autism spectrum disorder in sensory adapted environments were more likely to be relaxed during the medical visit than children who have an
autism spectrum disorder in offices with usual sights, sounds, and aromas (Cermak et al., 2015).

Interventions that reduce routine stress and anxiety-inducing environments have the potential for a ripple effect, positively influencing not only the child’s emotional regulation, but also the parental stress and anxiety levels.
CHAPTER 3: METHODS

Study Design

The study is a randomized controlled trial which contrasts the test intervention with a control group. Participants for the study included children aged 6-11 years old who have an autism spectrum disorder diagnosis. The participants and their parents were unaware of group assignments during the intervention.

Sample and Participant Selection

Patients aged 6 years to 11 years with any ASD diagnosis were eligible to participate. Although the median age for an autism spectrum disorder diagnosis is approximately four years old, higher functioning children who have an autism spectrum disorder may not receive a diagnosis until they are older (Christensen, D. L. 2016). The age at diagnosis also varies among differing populations, in part related to socioeconomic factors such as sex, race, and educational status (Fountain, King, & Bearman, 2011). To ensure a fully diverse sample, children younger than 6 years old were excluded. Children over the age of 11 were excluded, due to the potential impact of maturity on the child’s feelings of anxiety, which are the study outcomes.

Children who are nonverbal were able to participate in the study but were unable to provide data for all of the outcomes being measured. They completed the objective outcome measurements but did not complete the subjective outcome
measurements. There were no exclusions for children with altered cognitive functioning.

Twenty-eight patients (n=28) who visited participating clinics were selected and exposed to the intervention through an adaptive randomization process which was determined by the day of their appointment. The available appointment days during the intervention phase of the study were randomized using a random number table and all patients who fit the inclusion criteria and agreed to participate were either exposed to the intervention or the control as determined by appointment date.

Patients were included in the study if they had a medical office appointment for any reason during the intervention phase and agreed to participate. Upon arrival at their appointment, patients were given information about the study and informed consent forms to review with their usual intake paperwork. If they agreed to participate in the study, the parent signed the parental consent form and placed it in the clinic’s outgoing mail. The office staff were then notified of the decision to participate. The child then continued with the appointment as usual, with the addition of data collection and exposure to an essential oil of bergamot during the patient exam, if applicable.

In the patient room, baseline data were collected through administration of the State-Trait Anxiety Inventory for Children and a blood pressure cuff with heart rate monitor for participants. After baseline data were collected, participants in the experimental group were exposed to the aroma for the first 15 minutes of their check-
up, then post-intervention data were collected using the same measurements. After this was completed, the check-up continued as usual.

**IRB Approval**

This study was submitted to the Middle Tennessee State University’s IRB for evaluation and received approval in October of 2017 (protocol number 18-2057). IRB approval documents, including informed consent templates, can be found in Appendixes A and B.

**Recruitment and Randomization**

Children with an autism spectrum disorder experience situational anxiety and often endure increases in stress when placed in new situations or environments (Vasa et al., 2016). A medical office can increase the experience of anxiety among children who have an autism spectrum disorder, so this study took place in the medical office itself. Patients who participated in the study were selected if they had an appointment with a participating provider during the intervention period of the study and if they met the inclusion criteria. When they arrived, they were given an opportunity to choose to participate or to decline.

Randomization took place by date of the visit. Using adaptive randomization, the available appointment days during the intervention phase were categorized by intervention or control. Patients on the intervention days were exposed to the
bergamot essential oil for 15 minutes during their appointments between gathering baseline data and posttest data. Patients on the control days experienced the usual office smells and only completed the data collection process.

**Intervention**

The intervention took place immediately after the parents placed the signed consent in the outgoing mail and continued with the appointment. In the patient room, after baseline data were collected, if applicable, participants were exposed to the allocated aroma for 15 minutes while they waited in the room with their parents. After the exposure period ended, post-intervention data were collected on all participants and the visit continued as usual.

**Treatment Group**

The treatment group’s exposure consisted of undiluted cold-pressed bergamot essential oil (*Citrus bergamia*). This is the essential oil identified in the literature review as having the greatest potential for efficacy among this population with an overall aroma which is mild, generally regarded as pleasant.

Bergamot essential oil has consistently shown to reduce anxiety in pilot studies for various adult populations but has not been used in a study for children or for individuals with differing sensory experiences, such as children with ASD. The oil is cold pressed from an Italian citrus fruit and produces a light green color with a
citrus-like aroma. The citrus fragrance was unlikely to be recognized by the participants, as it is not a citrus commonly consumed in the US, and its mild fragrance made it suitable for children who have enhanced sensory experiences.

Chemically, the oil is somewhat similar to lavender essential oil, which is frequently used to reduce stress and anxiety in spa settings. However, clinical trials evaluating the efficacy of inhaled lavender essential oil have produced mixed results (Perry et al., 2012). Bergamot oil is rich in linalool, a monoterpenoid known for its pleasant aroma, but bergamot also contains limonene, the citrus-like monoterpenoid that causes it to have a fresh, citrus-like fragrance which is more enjoyable for children (Navarra et al., 2015). The participants who were randomized to the treatment group were exposed to 5 drops of the bergamot essential oil on an aromastick during the 15 minute intervention.

**Control Group**

The control group completed the baseline and follow-up survey but did not experience the essential oil. Placebos are highly effective for the reduction of symptoms of subjective measures such as pain perception and anxiety, compared to objective measures such as tumor size or blood sugar levels (Wechsler et al., 2011). Because this clinical trial was designed to evaluate the effects of an intervention on both objective and subjective outcomes, a comparison group was necessary to distinguish between the effects which can be actually attributed to the intervention.
itself, and the effects which were due to the mere practice of an aromatherapy intervention.

According to Estes et al. (2009), parents of children with an autism spectrum disorder experience far greater levels of parenting stress and psychological distress than parents of children with a developmental delay without an autism spectrum disorder. When compared to parents of typically developing children, the experience of parental stress for parents of children who have an autism spectrum disorder is far greater (Hayes et al., 2013). As the parents assisted in the completion of the STAI-CH survey, parental influence and perception of the exposure could have been influenced by a placebo-like effect, even in the absence of an actual placebo.

This control group provides data to distinguish which outcomes can be attributed to the aroma itself and which outcomes were due to the subjective perception. The control group did not experience any actual placebo. They received the provider’s usual care to serve as a comparison group and experienced the usual scents in the medical office.

**Materials**

The bergamot essential oil has been supplied by *Florihana*, a laboratory in France. Florihana specializes in extracting essential oils from crude plant matter and pressing vegetable oils from various plants. These oils were all supplied from the same batch, and the supplier has also provided the GC (gas chromatography) report...
for the essential oil, identifying the exact levels of the chemicals which are believed to provide medicinal actions. This report can be found in Appendix D.

**Administration of the Treatment**

Upon parental completion of informed consent, participants completed the STAI-CH for baseline data and were then exposed to the aroma, if applicable. Parents assisted the child with reading and responding to the questions on the STAI-CH, and parents actually marked the responses on the data sheets. There was no risk of crossover exposure between aromatherapy exposed patients and control patients because the exposure was randomized by day.

While the STAI-CH was being completed, baseline heart rate and blood pressure were collected by a care provider at the office, along with the usual intake procedures employed by each participating office. The data collected in the study include the participant’s blood pressure and heart rate. These were collected on provided medical record forms, which identified the patient using an arbitrary participant number that matches the consent form signed by the parents. To protect patient privacy, the participants were not identified by name and the medical provider maintained a record sheet that links the patient name with identification numbers should they need to access that information at a future date.

The treatment was administered through a personal inhalation device known as an “aromastick,” which is similar to a perfume tester strip. It consists of thick
paper upon which the drops of aromatic oil have been applied. The medical providers
gave a fresh aromastick to each patient who participated in the study and was
randomized to the intervention group. The aromastick was given to the child, if he or
she was curious about the scent in the room. If not, it was placed on the examining

table near the child or on the counter in the examining room. A timer was set outside
of the examining room for 15 minutes.

The study was not double blinded as the provider who is gathering baseline
and follow-up data was able to identify the aroma while gathering data simply due to
experience in the two rooms. Providers were notified of the randomization process
and which days to use the intervention. The prepared aromasticks were provided in a
sealed bag with the allocated oil already applied.

After the 15-minute exposure concluded, the provider collected the objective
measurements, and the patient completed a second STAI-CH. During this time, the
exposure to the aromastick was ongoing. After the treatment, the aromastick was
replaced in the sealed package and discarded. Survey and medical record data were
placed in a self addressed envelope and mailed to the researcher.

**Intent to Treat**

Because direct observation of provider fidelity to the randomization strategy
was not possible, the study was designed with an intent to treat design. This design
requires a conservative interpretation of treatment effect due to the potential for lack
of provider fidelity and noncompliance with the study protocol as designed. Provider fidelity was monitored through self-reporting, and the final analysis randomized each patient using the randomization calendar.

**Sample Size and Power**

Chang and Shen (2011) found that those who have higher to moderate anxiety scores are those who are the most likely to benefit from bergamot inhalation. In a similar study conducted in 2015 on 41 healthy adult women, bergamot essential oil was found to have a very large effect size of 1.15 (Watanabe et al., 2015).

A power analysis was performed using G*Power 3.1.9 to calculate the sample size that was required for the study. Because bergamot essential oil inhalation has been found to have a large effect size ($f = 1.15$), the un-inflated sample size required for analysis to detect a difference on STAI-CH scores was 11 participants, assuming a standard alpha of .95 (type 1 error of .05) and a power of .9 (type 2 error of .1).

Because the effect size found in previous studies is unusually large and previous studies are based on adult populations, the sample size was increased with a design effect of 2.5 to compensate for reductions in total effect size and failure of fidelity with the intent-to-treat design. With the possible loss of power due to the design effect of the study, the minimum sample size for this study was 28 patients.
Data Collection

Baseline data were collected from both treatment groups in the examining room prior to the start of the appointment. After the 15-minute intervention, data were collected again for analysis. Data collected include baseline and post-intervention heart rate, baseline and post-intervention blood pressure, and baseline and post-intervention scores on the State-Trait Anxiety Inventory for Children (STAI-CH). Medical record forms also gathered demographic information on the patients.

Measurement Instruments

The State-Trait Anxiety Inventory for Children (STAI-CH) is the instrument which was used to measure the immediate subjective experience of anxiety among participants in the study (See Appendix C). The complete STAI-CH contains 40 questions, 20 of which measure state anxiety, or how a child feels at a particular moment in time, and 20 of which measure trait anxiety, or general feelings of anxiety. As the purpose of this study was to evaluate the state experience of anxiety to obtain the immediate effects of the aroma, a modified STAI-CH which utilizes only the 20 state scores was used.

The scale used for this study contained 20 total questions which were measured on a 4-point Likert scale. Questions on the scale range from “I feel calm” and “I feel upset” to “I am tense” and “I am worried.” Scores range from 1, “not at all” to 4, “very much.” The questions were read either by the child or to the child by
their parent, and scores were recorded on the data entry sheets. The range of possible scores is from 20 to 60, with higher scores indicating higher levels of anxiety.

**Instrument Validity and Reliability**

To accurately measure state anxiety, the anxiety experienced by a child at a specific moment in time, the State-Trait Inventory for Children was used. This instrument, unlike many other anxiety screening tools, measures not only trait anxiety, but also state anxiety. This measurement is crucial as the study compared anxiety before and after the brief 15-minute intervention.

Because state anxiety is transitory in nature, test-retest is not an appropriate measure of reliability. Cronbach alpha, a more appropriate measure of internal consistency, of the S-scale (the state anxiety portion of the instrument) is .78 for males and .81 for females (Spielberger et al., 1973). Validity of the instrument has also been evaluated by item response theory and found to be highly discriminating with correlations between factor loadings and IRT slopes ranging from 0.95 to 0.98 (Kirisci et al., 1996). These validation assessments are on the general pediatric population and are not specific to children with an autism spectrum disorder, but the instrument has been used successfully to measure anxiety in children with autism in other studies which seek to identify interventions that may reduce anxiety (Corbett et al., 2016; Magiati et al., 2016).
Other measurement instruments used in this study included a blood pressure cuff and a heart rate monitor, and the providers used the existing equipment in their clinics to measure these outcomes. These measurements reflect state anxiety as physically expressed. In pediatric populations, heart rate and blood pressure have been found to be reliable measures of state anxiety, and heart rate among children with anxiety has been found to be both higher and less variable than controls (Monk et al., 2001; Jimeno et al., 2011).

Outcomes and Analysis

The outcomes measured included the change from baseline to the end of the study on all three measurement instruments. This provided two objective outcomes, blood pressure and heart rate, and a subjective outcome, STAI-CH.

The de-identified data collected in the study were analyzed to determine the extent to which exposure to the type of scent in the exam room had an effect on anxiety through blood pressure, heart rate, and patient perception as identified in the STAI-CH. Analysis included assessing whether environmental scent in exam rooms worsened or improved the anxiety that patients with ASD experienced while visiting medical providers.

Analysis of Covariance of the de-identified medical record data was conducted using SPSS. The dependent variable was the level of anxiety of the child at the end of the exam and the independent variable was the aromatherapy exposure or
lack thereof. The groups of children were identified as (1) those who are exposed to the scent of Bergamot, and (0) those who are exposed to usual scents, with intent-to-treat as the distinguishing factor.

Control variables included the child’s specific autism spectrum disorder diagnosis, the presence of a diagnosed anxiety disorder, child’s age, age at diagnosis, sex, insurance coverage, and the purpose of the child’s medical visit. Interaction models were tested in preliminary analysis.
CHAPTER 4: ANALYSIS AND RESULTS

Children with autism experience greater prevalence of anxiety than children who do not have autism (Kerns et al., 2014). This burden impacts society as a whole as well as children and their families individually (Buescher et al., 2014). Treatments for anxiety among children with autism are lacking, causing parents to turn to alternative solutions in the hopes of achieving some improvement in overall quality of life (Owen-Smith et al., 2015). The safety and efficacy of many CAM treatments for children with autism is not well established. There is a growing need for non-invasive solutions to the anxiety experienced by children with autism that are both safe and effective. The purpose of this study is to measure the effect of a non-invasive essential oil-based aromatic intervention on both subjective and objective anxiety scores among children ages 6-11 who have an autism spectrum disorder.

Participating Clinics

Eight clinics were recruited for participation during this study. Each of the participating clinics was selected due to a self-identified focus and practice emphasis on treating children with autism spectrum disorders. Each clinic expressed the ability to recruit approximately 8-12 patients during each month of the intervention period. These clinics are identified in Table 1.

Patient recruitment began November 9, 2017, and concluded March 9, 2018. Four of the clinics (Clinics 2, 4, 5, and 8) either did not see any patients who qualified
for the study during the study period or did not attempt to recruit any patients. The
other five clinics (Clinics 1, 3, 4, and 7) attempted to recruit patients and returned
patient data for the study.

A total of 37 patients were recruited to participate and 29 patients provided
consent to participate. Among those without consent, 3 declined participation, while 5
failed to return consent documents which were completed in full. An additional 4
patients were recruited by the doctors and provided consent but were outside of the
inclusion criteria age range, so they were excluded from the analysis. This leaves a
total of 25 patients who provided complete informed consent and met the inclusion
criteria (identified as Qualified Patients Recruited in Table 1).

<table>
<thead>
<tr>
<th>Clinic Number</th>
<th>State</th>
<th>Type of Practice</th>
<th>Qualified Patients Recruited</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Tennessee</td>
<td>Family Medicine, Pediatric Emphasis</td>
<td>3</td>
</tr>
<tr>
<td>2</td>
<td>Missouri</td>
<td>Chiropractic Medicine</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>Oregon</td>
<td>Pediatrics</td>
<td>1</td>
</tr>
<tr>
<td>4</td>
<td>Nevada</td>
<td>Pediatrics</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>Georgia</td>
<td>Pediatrics</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>North Carolina</td>
<td>Pediatrics</td>
<td>3</td>
</tr>
<tr>
<td>7</td>
<td>Indiana</td>
<td>Pediatrics</td>
<td>17</td>
</tr>
<tr>
<td>8</td>
<td>Oregon</td>
<td>Pediatrics</td>
<td>0</td>
</tr>
</tbody>
</table>
Participants were recruited during check-in for a scheduled appointment at a participating clinic. Upon check-in, the receptionist provided a qualifying patient’s parent(s) with the informed consent documents, which detailed the intervention and
the purpose of the study. (See Appendix B.) If a parent agreed to have the child participate, these documents were signed and mailed to the faculty advisor. When the child was taken to an exam room, baseline data were collected and the intervention was given, if appropriate to the child’s randomized group.

The patients in this study were primarily white males with private insurance (See Table 2). This is consistent with overall demographics for children with autism spectrum disorder (CDC, 2016). The mean age of the children was 8.54 (SD =1.9) years with a range of 6 years, 3 months to 11 years, 10 months.

**Patient Medical Background**

Every patient included in the analysis was diagnosed with an autism spectrum disorder prior to the intervention visit. Most of the patients had an autism diagnosis of Level 2 (requiring some support) on the DSM-V or the equivalent on the DSM-IV. Most of the children (80%) were visiting the practice for a routine autism-related pediatric visit. None of the children were visiting the clinic for a sick child visit, and the 16% were visiting as a follow-up to a sick visit. The purpose of the visit is unknown for one child. These results are displayed on Table 3.

The children in the study were diagnosed with autism between the ages of 18 months and 7 years, with a mean diagnosis age of 3.61 (SD=1.875). Only two (8%) children in the study also had a diagnosis of an anxiety disorder. This is unusual for
this population as approximately 40% of children with an autism spectrum disorder diagnosis also have an anxiety disorder diagnosis (van Steensel et al., 2011).

Table 3.

<table>
<thead>
<tr>
<th>Variable</th>
<th>$n$</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Autism Diagnosis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Level 1 or Equivalent</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Level 2 or Equivalent</td>
<td>18</td>
<td>72</td>
</tr>
<tr>
<td>Level 3 or Equivalent</td>
<td>4</td>
<td>16</td>
</tr>
<tr>
<td>Missing Data</td>
<td>3</td>
<td>12</td>
</tr>
<tr>
<td><strong>Purpose of Visit</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Routine Visit</td>
<td>20</td>
<td>80</td>
</tr>
<tr>
<td>Sick Visit</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Follow-Up from Sick Visit</td>
<td>4</td>
<td>16</td>
</tr>
<tr>
<td>Missing Data</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td><strong>Does the child have an anxiety diagnosis?</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>No</td>
<td>22</td>
<td>88</td>
</tr>
<tr>
<td>Unknown</td>
<td>1</td>
<td>4</td>
</tr>
</tbody>
</table>

**Patient Data**

Data collection included the patient’s demographic and health history information outlined above, baseline heart rate, baseline blood pressure, baseline
STAI inventory, posttest heart rate, posttest blood pressure, and posttest STAI inventory. Demographic information was provided by the MD or nurse who provided care for the child during the appointment. Heart rate and blood pressure were taken twice during the appointment, at baseline and at posttest, by the provider who attended the child. The STAI was completed by the child with parental assistance at baseline and again at posttest.

A total of 21 heart rate / blood pressure measurements were taken. The remaining 4 patients did not provide heart rate and blood pressure data because the child was too uncomfortable at the office visit to participate in the measurement.

A total of 22 baseline surveys were completed, and a total of 19 posttest surveys were completed. The remaining 3 patients were nonverbal and unable to complete the survey altogether. The 3 patients who completed the baseline but not the posttest did not provide details on why they declined the posttest survey.

**Randomization**

Patients were randomized through an adaptive randomization strategy. Each clinic was provided a calendar with instructions to identify intervention days and control days. The analysis for this study is intent to treat, so patients are assigned a group based on the calendar provided to each clinic. Based on the intent to treat classification of groups, there were 14 patients in the control group who did not receive any additional aromatic stimuli during the office visit and 11 patients in the
intervention group who experienced 15 minutes of the bergamot aromatic exposure at the start of their office visit. A crosstabs analysis of the demographic data, patient health history, and randomization groups reveals that there are no significant differences in demographics or health history among the intervention group and the control group. ANOVA analysis showed that there were no differences between the groups in systolic blood pressure, diastolic blood pressure, heart rate, age, age at diagnosis, and state-STAI-CH at baseline.

Data Analysis

Data were collected using hand written data-sheets which were distributed to participating clinics with the intervention materials. After these were returned by the clinics, the data were manually coded into SPSS for analysis. Data were first evaluated for accuracy, outliers, and normalcy.

**Research Question 1**: What effect does the environmental scent in a medical office patient examining room have on anxiety among children with autism spectrum disorders as measured by an anxiety inventory?

**Hypothesis 1**: When controlling for age, sex, and the presence of an anxiety diagnosis, children with an autism spectrum disorder who are exposed to bergamot essential oil during their medical appointments will have lower scores on the state anxiety scale than children who are not exposed to bergamot oil.
**STAI Analysis**

Total anxiety scores were measured subjectively through the State Trait Anxiety Inventory, using the state anxiety portion of the instrument, which includes 20 questions about state anxiety. Within this sub-scale, half of the questions are related to the presence of anxiety, while the other half are related to the absence of anxiety. Completion of the survey was defined as the completion of 18 or more of the 20 questions. A total of 22 baseline surveys were considered complete, and a total of 19 posttest surveys were considered complete.

Each question on the inventory offers 3 possible options, measured on a Likert scale. They center on the presence of a feeling and the options include a “very” and a “not” indicator for each feeling. For example, question one is, “I feel: 1. very calm, 2. calm, or 3. not calm” (Spielberger, 1973). Feelings which indicate the presence of anxiety are reverse coded so that the “very” indicator produces the highest score. This produces a total possible range of 20 to 60, with higher scores indicating higher levels of anxiety.

Responses were reverse coded, as applicable, and tallied to produce a total STAI score for all participants who completed 18 or more of the 20 questions on the inventory. The mean baseline response for the control group was 30.38 ($SD = 7.56$), while it was 30.55 ($SD = 3.62$) for the intervention group. The mean posttest response for the control group was 27.50 ($SD = 6.78$), and it was 33.64 ($SD = 8.37$) for the intervention group (see Table 4).
Control variables for this analysis include age, sex, and the presence of an anxiety diagnosis. Interactions between baseline variables and group assignment were assessed and found to be not significant. Preliminary checks were conducted to ensure that there were no violations of the assumptions of normality, linearity, homogeneity of variances, homogeneity of regression slopes, and reliable measurement of the covariate.

A one-way between-groups analysis of covariance was conducted to compare the effectiveness of the intervention of bergamot essential oil exposure on children who have an autism spectrum disorder. The independent variable was the exposure group (exposure to bergamot essential oil, control), and the dependent variable consisted of the total score on the STAI instrument after 15 minutes of either a control waiting period or the aromatic exposure. The covariate in this analysis was the total STAI score at the start of the exposure or control period in the medical office examining room.

### Table 4.

Mean and SD for Baseline and Posttest STAI

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Baseline Mean</th>
<th>SD</th>
<th>Posttest Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>30.38</td>
<td>7.56</td>
<td>27.50</td>
<td>6.78</td>
</tr>
<tr>
<td>Bergamot</td>
<td>30.55</td>
<td>3.62</td>
<td>33.64</td>
<td>8.37</td>
</tr>
</tbody>
</table>
After adjusting for baseline STAI scores, no significant difference was found between the intervention group and the control group on the posttest STAI score, $F(1, 16) = 3.839, p = .068$, partial eta squared = .194. Levene’s Test of Equality indicated that the assumption of homogeneity has not been violated ($F=0.052, p=0.822$). Evaluation of the residuals found that they were normally distributed.

There was a relationship between the baseline and the posttest score on the STAI, as indicated by a partial eta squared value of .32 (see Table 5).

### Table 5.

ANCOVA of Posttest STAI with Baseline STAI as Covariate

<table>
<thead>
<tr>
<th>Source</th>
<th>$df$</th>
<th>SS</th>
<th>MS</th>
<th>$F$</th>
<th>$p$</th>
<th>$\eta^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline STAI</td>
<td>1</td>
<td>327.22</td>
<td>327.22</td>
<td>7.53</td>
<td>0.014</td>
<td>0.32</td>
</tr>
<tr>
<td>Bergamot Exposure</td>
<td>1</td>
<td>166.83</td>
<td>166.83</td>
<td>3.84</td>
<td>0.068</td>
<td>0.19</td>
</tr>
<tr>
<td>Error</td>
<td>16</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>19</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Adjusted R Squared = .346

### Results

Based on the findings of this study, the hypothesis that children who are exposed to bergamot essential oil during their medical appointments will have lower scores on the state anxiety scale than children who are not exposed to bergamot oil was not supported by the results. According to these data, it was concluded that children who are exposed to bergamot essential oil during the first 15 minutes of the
time spent in a medical examining room score about the same on the STAI instrument than children who are not exposed to bergamot essential oil during the first 15 minutes of the time spent in a medical examining room.

**STAI Sub-scale Analyses**

Further analysis, including Cronbach alpha, of the participant responses indicates that the baseline data have very little variation on the presence of anxiety questions. This limits the overall variation of responses on the STAI total scores. This is consistent with mean score totals provided by studies identifying the validity of the instrument (Speilberger, 1973).

Possible scores on the total of presence of anxiety questions range from 10 to 30. The majority \( n = 16; 84\% \) of the patients reported a 10 or 11 on the sub-scale at baseline. As a result, the scale was divided into its two sub-scales for further analysis on the sub-scale which evaluates the absence of anxiety related symptoms. This resulted in the creation of an alternative hypothesis #1.

**Alternative Question 1**: What effect does the environmental scent in a medical office patient examining room have on anxiety among children with autism spectrum disorders as measured by the absence of anxiety scores on the STAI anxiety inventory?
Hypothesis 1: When controlling for age, sex, and the presence of an anxiety diagnosis, children with an autism spectrum disorder who are exposed to bergamot essential oil during their medical appointments will have lower absence of anxiety scores on the state anxiety scale than children who are not exposed to bergamot oil.

For this analysis, the ten questions related to the absence of anxiety related feelings on the state portion of the STAI-CH measurement was used. Completion of the survey was defined as the completion of 9 or more of the 10 questions. A total of 22 baseline surveys were completed, and a total of 18 posttest surveys were completed.

Table 6.
Mean and SD for Baseline and Posttest STAI for Absence of Anxiety ($n = 18$)

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Baseline Mean</th>
<th>SD</th>
<th>Posttest Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>18.86</td>
<td>5.84</td>
<td>16.71</td>
<td>6.45</td>
</tr>
<tr>
<td>Bergamot</td>
<td>19.45</td>
<td>2.94</td>
<td>21.18</td>
<td>4.67</td>
</tr>
</tbody>
</table>

Responses were tallied to produce a total STAI score for all participants who completed 9 or more of the 10 questions on the inventory. This produces a total possible range of 10 to 30, with higher scores indicating higher levels of anxiety. The mean baseline response for the control group was 18.86 ($SD = 5.84$), while it was 19.45 ($SD = 2.94$) for the intervention group. The mean posttest response for the
control group was 16.71 \( (SD = 6.45) \), and it was 21.18 \( (SD = 4.67) \) for the intervention group (see Table 6).

**ANCOVA**

Control variables for this analysis include age, sex, and the presence of an anxiety diagnosis. Interactions between baseline characteristics and group assignment were assessed and found to be not significant. Preliminary checks were conducted to ensure that there were no violations of the assumptions of normality, linearity, homogeneity of variances, homogeneity of regression slopes, and reliable measurement of the covariate.

A one-way between-groups analysis of covariance was conducted to compare the effectiveness of the intervention of bergamot essential oil exposure on children who have an autism spectrum disorder. The independent variable was the exposure group (exposure to bergamot essential oil, control), and the dependent variable consisted of the total score on the sub-scale of the STAI instrument after 15 minutes of either a control waiting period or the aromatic exposure. The covariate in this analysis was the total STAI sub-scale score at the start of the exposure or control period in the medical office examining room.

After adjusting for baseline STAI scores, there was a significant difference between the intervention group and the control group on the posttest sub-scale STAI score, \( F(1,15) = 4.568, p = 0.049 \), partial eta squared = .233 (see Table 7). Levene’s
Test of Equality indicated that the assumption of homogeneity has not been violated \((F = 0.126; p = .727)\). Evaluation of the residuals found that they were normally distributed. Children who were exposed to bergamot essential oil had somewhat higher mean scores on the STAI-CH absence of anxiety sub-scale than children who were not exposed to bergamot essential oil.

<table>
<thead>
<tr>
<th>Source</th>
<th>(df)</th>
<th>SS</th>
<th>MS</th>
<th>(F)</th>
<th>(p)</th>
<th>(\eta^2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline STAI Sub-scale</td>
<td>1</td>
<td>253.37</td>
<td>253.37</td>
<td>17.785</td>
<td>0.001</td>
<td>0.542</td>
</tr>
<tr>
<td>Bergamot Exposure</td>
<td>1</td>
<td>65.08</td>
<td>65.08</td>
<td>4.568</td>
<td>0.049</td>
<td>0.233</td>
</tr>
<tr>
<td>Error</td>
<td>15</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>18</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Adjusted R Squared = .562*

**Results**

Based on the results of this study, the hypothesis that children who are exposed to bergamot essential oil during their medical appointments will have lower scores on the STAI absence of anxiety sub-scale than children who are not exposed to bergamot oil was not supported by the results. According to these data, it was concluded that children who are exposed to bergamot essential oil during the first 15 minutes of the time spent in a medical examining room score higher on the STAI absence of anxiety sub-scale than children who are not exposed to bergamot essential
oil during the first 15 minutes of the time spent in a medical examining room. This indicates that children who are exposed to bergamot essential oil have much greater levels of anxiety than children who are not exposed to bergamot essential oil, specifically as measured through the absence of anxiety items on the scale.

**Heart Rate Analysis**

Total anxiety scores were measured objectively through heart rate and blood pressure both before and after the intervention. These scores were also analyzed for research questions 2 and 3.

**Research Question 2:** What effect does the environmental scent in a medical office patient examining room have on anxiety among children with autism spectrum disorders as measured by heart rate?

**Hypothesis 2:** When controlling for age, sex, and the presence of an anxiety diagnosis, children with an autism spectrum disorder who are exposed to bergamot essential oil during their medical appointments will have lower heart rates than children who are not exposed to bergamot oil.

A total of 21 baseline heart rate levels, and a total of 21 posttest heart rate levels were taken. The mean baseline heart rate for the control group was 92.73 ($SD = 14.37$), while it was 96.1 ($SD = 7.75$) for the intervention group. The mean posttest heart rate for the control group was 94.55 ($SD = 15.74$), and it was 96.2 ($SD = 8.97$) for the intervention group (see Table 8).
ANCOVA

Control variables for this analysis include age, sex, and the presence of an anxiety diagnosis. Interactions between baseline characteristics and group assignment were assessed and not found to be significant. Preliminary checks were conducted to ensure that there were no violations of the assumptions of normality, linearity, homogeneity of variances, homogeneity of regression slopes, and reliable measurement of the covariate.

A one-way between-groups analysis of covariance was conducted to compare the effectiveness of the intervention of bergamot essential oil exposure on children who have an autism spectrum disorder. The independent variable was the exposure group (exposure to bergamot essential oil, control), and the dependent variable was the heart rate after 15 minutes of either a control waiting period or the aromatic exposure. The covariate in this analysis was the heart rate at the start of the exposure or control period in the medical office examining room.

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Baseline M</th>
<th>Baseline SD</th>
<th>Posttest M</th>
<th>Posttest SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>92.73</td>
<td>14.37</td>
<td>94.55</td>
<td>15.74</td>
</tr>
<tr>
<td>Bergamot</td>
<td>96.10</td>
<td>7.75</td>
<td>96.20</td>
<td>8.97</td>
</tr>
</tbody>
</table>

Table 8.
Mean and SD for Baseline and Posttest Heart Rate (n = 21)
After adjusting for baseline heart rate, there was no significant difference between the intervention group and the control group’s posttest heart rate, $F(1, 18) = 0.003, p = .957$, partial eta squared $= .000$. Levene’s Test of Equality indicated that the assumption of homogeneity has not been violated ($F = 2.07, p = .167$). Evaluation of the residuals found that they were normally distributed. There was a small relationship between the baseline heart rate and the posttest heart rate, as indicated by a partial eta squared of .266 (see Table 9).

### Table 9.

**ANCOVA of Posttest Heart Rate with Baseline Heart Rate as Covariate**

<table>
<thead>
<tr>
<th>Source</th>
<th>df</th>
<th>SS</th>
<th>MS</th>
<th>F</th>
<th>p</th>
<th>η²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline Heart Rate</td>
<td>1</td>
<td>851.57</td>
<td>851.57</td>
<td>6.520</td>
<td>0.020</td>
<td>0.269</td>
</tr>
<tr>
<td>Bergamot Exposure</td>
<td>1</td>
<td>0.38</td>
<td>0.38</td>
<td>0.003</td>
<td>0.957</td>
<td>0.000</td>
</tr>
<tr>
<td>Error</td>
<td>18</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>21</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Adjusted R Squared = .188*

### Results

Based on the results of this study, Hypothesis #2, which stated that the children who are exposed to bergamot essential oil during their medical office visits will have lower posttest heart rates than children who were not exposed to bergamot essential oil during their office visits was not supported by the results. Based on these data, it was concluded that there were no differences in total posttest heart rate
between children who are exposed to bergamot essential oil during the first 15 minutes of the time spent in a medical examining room and children who are not exposed to bergamot essential oil during the first 15 minutes of the time spent in a medical examining room. Children who were exposed to the essential oil had similar heart rates to children who were not exposed to the essential oil.

**Blood Pressure Analysis**

To assess research question 3 and hypothesis 3, diastolic and systolic figures were analyzed individually, resulting in two separate analyses.

**Research Question 3:** What effect does the environmental scent in a medical office patient examining room have on anxiety among children with autism spectrum disorders as measured by blood pressure?

**Hypothesis 3:** When controlling for age, sex, and the presence of an anxiety diagnosis, children with an autism spectrum disorder who are exposed to bergamot essential oil during their medical appointments will have lower blood pressure readings than children who are not exposed to bergamot oil.

A total of 23 baseline blood pressure levels, and a total of 21 posttest blood pressure levels were taken. The mean baseline blood pressure for the control group was 102.18 (SD = 11.01) over 62 (SD = 9.51), while it was 95.5 (SD = 5.28) over 62.4 (SD = 5.78) for the intervention group. The mean posttest blood pressure for the
control group was 102 (SD = 11.28) over 66.0 (SD = 8.76), and it was 98.1 (SD = 8.67) over 63.6 (SD = 4.6) for the intervention group (see Table 10).

**Table 10.**

Mean and SD for Baseline and Posttest Blood Pressure *(n = 21)*

<table>
<thead>
<tr>
<th>Exposure</th>
<th>M</th>
<th>SD</th>
<th>M</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control Systolic</td>
<td>102.18</td>
<td>11.01</td>
<td>102.00</td>
<td>11.28</td>
</tr>
<tr>
<td>Control Diastolic</td>
<td>62.00</td>
<td>9.51</td>
<td>66.00</td>
<td>8.76</td>
</tr>
<tr>
<td>Bergamot Systolic</td>
<td>95.50</td>
<td>5.28</td>
<td>98.10</td>
<td>8.70</td>
</tr>
<tr>
<td>Bergamot Diastolic</td>
<td>62.40</td>
<td>5.78</td>
<td>63.60</td>
<td>4.60</td>
</tr>
</tbody>
</table>

**ANCOVA for Systolic Blood Pressure**

Control variables for this analysis include age, sex, and the presence of an anxiety diagnosis. Interactions were assessed and not found to be significant. Preliminary checks were conducted to ensure that there were no violations of the assumptions of normality, linearity, homogeneity of variances, homogeneity of regression slopes, and reliable measurement of the covariate.

A one-way between-groups analysis of covariance was conducted to compare the effectiveness of the intervention of bergamot essential oil exposure on children who have an autism spectrum disorder. The independent variable was the exposure group (exposure to bergamot essential oil, control), and the dependent variable was the blood pressure after 15 minutes of either a control waiting period or the aromatic
exposure. The covariate in this analysis was the systolic blood pressure at the start of
the exposure or control period in the medical office examining room.

Table 11.

<table>
<thead>
<tr>
<th>Source</th>
<th>df</th>
<th>SS</th>
<th>MS</th>
<th>F</th>
<th>p</th>
<th>η (2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline Systolic</td>
<td>1</td>
<td>512.326</td>
<td>512.326</td>
<td>6.40</td>
<td>0.021</td>
<td>0.262</td>
</tr>
<tr>
<td>Bergamot Exposure</td>
<td>1</td>
<td>0.014</td>
<td>0.014</td>
<td>0.00</td>
<td>0.990</td>
<td>0.000</td>
</tr>
<tr>
<td>Error</td>
<td>18</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>21</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Adjusted R Squared = .213

After adjusting for baseline systolic heart rate, there was no significant
difference between the intervention group and the control group’s posttest systolic
blood pressure, $F(1, 18) = 0.000, p = .990$, partial eta squared = .000. Levene’s Test
of Equality indicated that the assumption of homogeneity has not been violated ($F =
0.039, p = .845$). Evaluation of the residuals found that they were normally
distributed. There was a relationship between the baseline systolic blood pressure and
the posttest systolic blood pressure, as indicated by a partial eta squared of .262 (see
Table 11).
ANCOVA for Diastolic Blood Pressure

Control variables for this analysis include age, sex, and the presence of an anxiety diagnosis. Interactions between baseline characteristics and group assignment were assessed and not found to be significant. Preliminary checks were conducted to ensure that there were no violations of the assumptions of normality, linearity, homogeneity of variances, homogeneity of regression slopes, and reliable measurement of the covariate.

A one-way between-groups analysis of covariance was conducted to compare the effectiveness of the intervention of bergamot essential oil exposure on children who have an autism spectrum disorder. The independent variable was the exposure group (exposure to bergamot essential oil, control), and the dependent variable was the blood pressure after 15 minutes of either a control waiting period or the aromatic exposure. The covariate in this analysis was the diastolic blood pressure at the start of the exposure or control period in the medical office examining room.

After adjusting for baseline diastolic heart rate, there was no significant difference between the intervention group and the control group’s posttest diastolic blood pressure, $F (1, 18) = 1.21, p = .286$, partial eta squared = .063. Levene’s Test of Equality indicated that the assumption of homogeneity has not been violated ($F = 0.128, p = .724$). Evaluation of the residuals found that they were normally distributed. There was a relationship between the baseline diastolic blood pressure
and the posttest diastolic blood pressure, as indicated by a partial eta squared of .436 (see Table 12).

Table 12.

<table>
<thead>
<tr>
<th>Source</th>
<th>df</th>
<th>SS</th>
<th>MS</th>
<th>F</th>
<th>p</th>
<th>η 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline Diastolic</td>
<td>1</td>
<td>418.08</td>
<td>418.08</td>
<td>13.93</td>
<td>0.002</td>
<td>0.436</td>
</tr>
<tr>
<td>Bergamot Exposure</td>
<td>1</td>
<td>36.36</td>
<td>36.36</td>
<td>1.21</td>
<td>0.286</td>
<td>0.063</td>
</tr>
<tr>
<td>Error</td>
<td>18</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
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<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Adjusted R Squared = .393*

Results

Based on the results of this study, Hypothesis #3, which stated that the children who are exposed to bergamot essential oil during their medical office visits will have lower posttest blood pressure scores than children who were not exposed to bergamot essential oil during their office visits was not supported by the results. Based on these data, it was concluded that there were no differences in total posttest blood pressure between children who are exposed to bergamot essential oil during the first 15 minutes of the time spent in a medical examining room and children who are not exposed to bergamot essential oil during the first 15 minutes of the time spent in a medical examining room. Children who were exposed to the essential oil had similar blood pressure scores to children who were not exposed to the essential oil.
Summary

To answer the research questions posed, eight clinics participated in recruiting patients for the study. A total of 25 patients from 4 clinics participated in the study, which began November 9, 2017, and concluded March 9, 2018. The patients in this study were primarily white males with private insurance. This is consistent with overall demographics for children with autism spectrum disorder (CDC, 2016). The mean age of the children was 8.54 (SD = 1.9) years with a range of 6 years, 3 months to 11 years, 10 months.

Every patient included in the analysis was diagnosed with an autism spectrum disorder prior to the intervention visit. Most of the patients had an autism diagnosis of Level 2 (requiring some support) on the DSM-V or the equivalent on the DSM-IV. Most of the children (80%) were visiting the practice for a routine autism-related pediatric visit. None of the children were visiting the clinic for a sick child visit, and the 16% were visiting as a follow-up to a sick visit. The purpose of the visit is unknown for one child.

The study consisted of a 15-minute exposure to bergamot essential oil at the start of the visit, once the child was in the medical examining room. Before the exposure, a provider from a participating clinic took the child’s blood pressure and heart rate, and provided the child a STAI-CH state anxiety survey to collect baseline data. After 15 minutes, the provider took posttest blood pressure and heart rate
readings and provided another STAI-CH state anxiety survey for posttest data. Parents assisted the children in completing the survey, if needed.

ANCOVA analysis was conducted to evaluate the differences in posttest scores using baseline scores as a covariate. To answer the research question, a total of five ANCOVA analyses were conducted. These evaluated changes from baseline to posttest in both diastolic and systolic blood pressure, heart rate, the STAI-CH inventory, and the portion of the STAI-CH inventory which evaluates the absence of anxiety feelings.

Preliminary analyses of the data indicated that there were no significant interactions and none of the assumptions required for ANCOVA were violated. For all of the objective outcomes (diastolic, systolic, and heart rate), there was no difference between the intervention group and the control group. After adjusting for baseline scores, children who inhaled the scent of the bergamot essential oil during the 15 minute period had similar heart rate and blood pressure readings as children who did not inhale the scent of the bergamot essential oil.

For the subjective perception of anxiety, outcomes differed. When the total STAI-CH inventory was analyzed, children who inhaled the scent of bergamot essential oil during the first 15 minutes of their medical appointments had anxiety scores which were similar to children who did not inhale the essential oil. Additional analysis revealed little to no variation in the portion of the state anxiety scale which
analyzed the presence of anxiety related feelings, so both sub-scales of the state anxiety scale were evaluated separately to identify any changes between the groups.

When the portion of the inventory which evaluated the absence of anxiety related feelings was evaluated, it was also found that children who inhaled bergamot essential oil during the first 15 minutes of their medical appointments had somewhat higher scores than children who did not inhale the scent of the essential oil. The total range of scores on the absence of anxiety sub-scale is from 10 to 30, with higher levels indicating greater anxiety. Children who were exposed to the essential oil had mean scores of 21.18 ($SD = 4.67$) while children who were not exposed had mean scores of 16.71 ($SD = 6.45$).

Based on the findings of this study, exposure to the essential oil during the first 15 minutes of a medical office appointment results in a greater perception of anxiety for children who have an autism spectrum disorder. Exposure to the essential oil during this time does not appear to have an impact on objective measurements of anxiety, such as blood pressure or heart rate.
CHAPTER 5: CONCLUSIONS AND RECOMMENDATIONS

Introduction to Autism Spectrum Disorder

Autism is a psychological condition which impacts individuals of all ages and is typically diagnosed in early childhood (CDC, 2016). There are multiple diagnoses which exist on the spectrum of autism disorders, all of which impact an individual’s ability to thrive in a social context. These deficits include social-emotional reciprocity, nonverbal communication, and social relationships. Other symptoms include restrictive, repetitive patterns of behavior including an insistence on sameness and hyper- or hypo reactivity to sensory input (DSM-V, 2013).

Children with an autism spectrum disorder experience both typical anxiety symptoms and atypical anxiety symptoms, which are explained through behaviors that do not reflect DSM definitions. In one sample, 48% of children experienced traditional anxiety disorders while 46% of children experienced anxiety symptoms which are not consistent with psychological disorders related to anxiety found in the DSM (Kerns et al., 2014). These anxiety symptoms can be predicted by variables related to ASD traits, with children who are higher functioning experiencing lower levels of anxiety.

Treatment

Existing treatment goals focus on addressing the most pressing symptoms and improving overall quality of life for individuals who live with an autism spectrum
disorder. The most pressing needs identified in the literature are those related to quality of life, such as social support, anxiety and stress relief, and emotional regulation (White et al., 2016).

Treatments for anxiety among children with an autism spectrum disorder are lacking, causing parents to turn to alternative solutions in the hopes of achieving some improvement in overall quality of life (Owen-Smith et al., 2015). Two underlying problems persist across treatments for anxiety among children who have an autism spectrum disorder. These include a lack of efficacy and high incidence of adverse events (Vasa et al., 2014). Noninvasive solutions for anxiety have frequently been found to be ineffective, while stronger pharmaceutical interventions carry high incidence of adverse events, while failing to achieve efficacy that can be documented in the literature. The safety and efficacy of many complementary and alternative medical treatments for children with an autism spectrum disorder are not well established, and there is a growing need for non-invasive solutions to the anxiety experienced by children with an autism spectrum disorder that are both safe and effective.

Aromatherapy through the use of bergamot essential oil is a CAM related therapy that poses minimal risk and has the potential to offer noninvasive treatment for symptoms such as anxiety. The effects of inhaled bergamot oil for anxiety have been documented in the literature, but not specifically on children who have an autism spectrum disorder (Chang & Shen, 2011; Ndao et al., 2012; Ni et al., 2013).
The Current Study

This study seeks to evaluate the role of a sensory enhanced environment through the use of bergamot essential oil as a tool to improve both problem-focused coping and emotional regulation of children with an autism spectrum disorder who require routine medical visits. The study is a randomized controlled trial which contrasts the test intervention with a control group, with adaptive randomization utilized for group assignment. Participants for the study included children aged 6-11 years old who have an autism spectrum disorder diagnosis. Demographic data were collected to identify sex, age, age at autism diagnosis, insurance type, and the presence of an anxiety disorder.

After providing informed consent, participants in the treatment arm of the study were exposed to bergamot essential oil for 15 minutes in the medical examining room. Baseline heart rate, blood pressure, and scores on the State Trait Anxiety Inventory for Children (STAI-CH) were collected. These scores were also collected after the 15-minute intervention. The outcomes being measured include the changes from baseline to the end of the study on all three measurement instruments. This provides two objective outcomes, blood pressure and heart rate, and a subjective outcome, STAI-CH.
Conclusions

A total of 25 patients from 4 clinics participated in the study, which began November 9, 2017, and concluded March 2, 2018. Every patient in the study has previously been diagnosed with an autism spectrum disorder. The patients in this study were primarily white males with private insurance with a mean age of 8.54 years (SD of 1.89).

ANCOVA analyses were conducted to answer the research questions. These evaluated changes from baseline to posttest in both diastolic and systolic blood pressure, heart rate, the STAI-CH inventory, and the portion of the STAI-CH inventory which evaluates the absence of anxiety feelings.

Preliminary analyses of the data indicated that there were no significant interactions and none of the assumptions required for ANCOVA were violated. There was no difference between intervention and control outcomes on objective measurements of blood pressure and heart rate. After adjusting for baseline scores, children who inhaled the bergamot essential oil during the 15 minute period had similar heart rate and blood pressure readings as children who did not inhale the bergamot essential oil.

When the perception of anxiety data were analyzed, it was found that children who inhaled the scent of bergamot essential oil during the first 15 minutes of their medical appointments had similar scores as compared to children who did not inhale the scent of the essential oil. The state portion of the STAI-CH instrument contains
two sub-scales. When the portion of the inventory which evaluated the absence of anxiety related feelings was evaluated, it was also found that children who inhaled bergamot essential oil during the first 15 minutes of their medical appointments had somewhat higher scores than children who did not inhale the essential oil. Absence of anxiety STAI-CH scores range from 10 to 30 with higher scores indicating higher feelings of anxiety. Children who were exposed to the essential oil had mean scores of 21.18 ($SD = 4.67$) while children who were not exposed had mean scores of 16.71 ($SD = 6.45$).

This study provides evidence that exposure to bergamot essential oil at a medical office produces increased feelings of anxiety for children who have been diagnosed with an autism spectrum disorder. Exposure to the essential oil during this time does not appear to have an impact on blood pressure or heart rate for children who have been diagnosed with an autism spectrum disorder.

**Discussion**

The findings of this study differ from previous findings regarding the use of bergamot essential oil to treat medical office-induced anxiety. However, this is the first study to evaluate bergamot essential oil as an anxiolytic within a population of children who have been diagnosed with an autism spectrum disorder. Children who have an autism spectrum disorder experience sensory hypersensitivity and chronic levels of anxiety. Each of these underlying factors, or a combination of the two, may
explain why tools which have been found to be effective in a general population may not be effective, and may even be harmful, in this population.

**Sensory Hypersensitivity**

Sensory hypersensitivity is experienced by up to 88% of children who are diagnosed with an autism spectrum disorder (Baum et al., 2015). Sensory abnormalities are so intertwined with autism spectrum disorders that one of the diagnostic criteria include, “hyper- or hypo-reactivity to sensory input or unusual interest in sensory aspects of the environment” (DSM-V, 2013). Adults with an autism spectrum disorder diagnosis have been found to perceive odors to be more intense and less pleasant than controls who do not have an autism spectrum disorder diagnosis (Wicker et al., 2016).

While both hypo- and hypersensitivity exist among individuals who have an autism spectrum disorder, discriminating factors appear to include age and presence of autistic traits in an individual (Larsson et al., 2017; Muratori et al., 2017; Baum et al., 2015). There is a clear relationship between the sensitivity to sensory experiences and the level of autism in a child, which is relevant in light of the health history of children in this study, all of whom had level 2 or 3 autism diagnoses on the DSM-V, or the equivalent on the DSM-IV. Researchers found that individuals with a greater number of autistic traits were more sensitive to olfactory exposures than individuals with fewer autistic traits, in addition to finding that individuals with an autism
spectrum disorder could detect aromas at a greater distance than control individuals who did not have an autism spectrum disorder (Ashwin et al., 2014). This is consistent with previous work on the relationship between autistic traits and olfactory experiences (Galle et al., 2013).

Hypersensitivity to sensory experiences has also been linked with anxiety in children who have autism. Researchers have found that hypersensitivity is increased after exposure to sensory stimuli (Green et al., 2015). As such, introducing an additional olfactory exposure has the potential to increase, rather than decrease anxious feelings among this population. Children with an autism spectrum disorder may already be hypersensitive to sensory experiences, with reactivity heightened by the myriad of sensory exposures which are already present in a medical office. Adding an aroma during this time may be compounding the issue further. Future studies should evaluate the potential for bergamot or another essential oil to reduce anxiety in environments which are not already saturated with new and unfamiliar sensory experiences.

Presence of Chronic Anxiety

In addition to hypersensitive sensory experiences, children who have an autism spectrum disorder also have underlying chronic feelings of anxiety. Anxious feelings are common among all populations in stressful situations, but stress differs from clinical anxiety (DSM-V, 2013). Previous studies have evaluated the use of
essential oils for stressful situations which produce feelings of anxiety, but not for stressful situations among populations which also have an anxiety disorder or chronic anxiety as a result of a diagnosis of an autism spectrum disorder. Populations which have an anxiety disorder, chronic anxiety, and anxious feelings due to stress may respond differently to interventions designed to reduce symptoms of anxiety.

Demographic Differences

Additionally, autism spectrum disorders affect males in greater proportion than females (CDC, 2016). Much of the previous work on the use of bergamot for anxiety has been conducted primarily on females. This is consistent with the overall burden of anxiety, but not the distribution of autism spectrum disorders (McLean et al., 2011). In the past, multiple researchers have called for gender-specific treatment of anxiety, rather than gender-neutral treatment (Bekker & van Mens-Verhulst, 2007). While controlling for sex did not impact the findings of this study, the sample for this study only included 4 females, producing a sex-distribution within the sample which differs substantially from previous work on the efficacy of the essential oil via inhalation.

Recommendations for Practice

While essential oils remain valuable tools for a reduction in stress-induced feelings of anxiety among a general population, children who have an autism
spectrum disorder or any condition with underlying chronic anxiety may not benefit from the essential oils which are found to reduce anxiety in other studies.

Furthermore, the use of anxiolytic essential oils on a population of children who have been diagnosed with an autism spectrum disorder may have the unintended effect of actually increasing, rather than decreasing feelings of anxiety, according to the findings of this study.

It is also noteworthy that the increase in anxiety scores was only found on the subjective scale but not on the objective analysis of blood pressure and heart rate.

There is evidence to support the idea that the variability of resting heart rate is reduced among individuals who have an anxiety disorder, but the stimuli of the stress-inducing medical appointment would be sufficient to trigger anxious feelings that produce some variation (Chalmers et al., 2016). Additionally, it is possible that the unfamiliar aroma used for this study was merely found to be unenjoyable by the children who participated. Responses may differ if a more familiar scent, such as orange, was used for this research. Additional studies should be conducted to evaluate the role of personal preference on subjective and objective outcomes for aromatherapy and anxiety among children with autism.

**Study Limitations**

This study has several limitations. The intent to treat model, combined with the geographic diversity precluded closer oversight on provider fidelity to the
treatment model. Based on self-reporting of the participating providers, fidelity was confirmed in 17 of the 25 cases or 68%. In 5 cases (20%), self-reporting of group assignment did not match randomization allocation, and in 3 cases (12%), self-reporting of assignment was absent from the data. Many of the cases which lacked provider fidelity were also cases which provided incomplete data.

Additionally, while the geographic diversity of the patient population was a strength, the poor response and lack of diversity among participating clinics produced a small sample with a single clinic overrepresented in the sample. A more robust sample of children who have an autism spectrum disorder from across the country may yield differing results. Additionally, this sample did not represent the prevalence of an anxiety diagnosis which is identified in the literature.

The study focused on data collection regarding the proposed research questions and did not ask any open-ended questions to provide additional details on the subjective experience of aromatherapy exposure among the participating children. This prohibited the analysis from controlling for personal preference or drawing conclusions about the role of personal preference in the ultimate outcomes. Similarly, the parents assisted the children with completion of the STAI during the baseline and posttest. Parental involvement in the completion of the instrument may influence the final score.
**Recommendations for Future Research**

Given previous findings that the oil has been found to improve parasympathetic nervous system activity with a reduction in salivary cortisol levels after inhalation exposure, the mechanisms of action by which this oil affects a child who has an autism spectrum disorder is worth exploring (Watanabe et al., 2015). Children who have autism spectrum disorders experience significantly greater cortisol responses to routine medical procedures, such as a blood draw, as compared to children who do not have an autism spectrum disorder (Spratt et al., 2012). As such, it would reason that an essential oil with the capability of reducing cortisol levels which have increased due to stressors would be particularly beneficial for children with an autism spectrum disorder. This study did not measure salivary cortisol levels among children, but future research should evaluate this outcome.

**Aromatherapy Mechanism of Action**

Traditional aromatherapy approaches suggest that some of the effects of essential oils are due to scent memory (Lis-Balchin, 2006). According to this theory, the aroma from a substance enters the body via inhalation and the olfactory stimuli reaches a group of structures in the brain collectively referred to as the limbic system, where the scent is capable of impacting emotions and memory. Both the amygdala and hypothalamus are included in this group of structures, and both of these structures
are known to be affected by aromatic stimuli (Soundry et al., 2011; Zald & Pardo, 1997).

The effect of olfactory stimuli as a cue for triggering autobiographical memories has been found to be stronger than visual stimuli (de Bruijn et al., 2018). Based on this theoretical mechanism of action, an individual’s scent memory would have to first be primed with a calming aroma, combined with a pleasant experience to produce an association between the scent and feelings of security. According to traditional aromatherapy theory, this aroma would then be capable of producing calming feelings when introduced at a later date.

As such, a fresh exposure to a new aroma would not be sufficient to bring about a calming response. While this is not the mechanism of action utilized in previous studies on the anxiety reducing actions of essential oils among individuals in the general population, future studies should explore the potential for a primed scent memory approach to anxiety reduction among children who have an autism spectrum disorder.

**Mixed Methods Designs**

This study found that the perception of anxiety increased while objective measures of anxiety (blood pressure and heart rate) stayed the same among the intervention and control group. Additional research may evaluate the lived experience of a child who has been diagnosed with an autism spectrum disorder and the
experience of an additional aromatic sensory experience at a medical office through mixed-methods approaches. This study did not ask the child whether or not they liked the aroma of the oil or collect any open-ended or qualitative data on the child’s experience. As the aroma selected for the study is an unfamiliar scent, the newness of the aroma may have created a heightened sense of anxiety that would not be replicated by a more familiar aroma or the ability of the child to select their preferred scent.

**Future Research**

The oil for this study was selected based on previous research which was primarily conducted on females who do not have an autism spectrum disorder. Essential oils appear to have a positive influence on the perception of anxiety, according to previous findings, but the specific oil selection that was found to be effective in other populations achieved the opposite result in this study. Additional studies with different selections of essential oils are warranted to evaluate whether or not the effect found in this study is due to the oil selection or the presence of an additional aromatic sensory experience. Additionally, while this study was sufficiently powered, larger studies may be able to identify variables which specify subpopulations within this sample population who respond differently to the aromatic exposure.
Conclusion

The use of bergamot essential oil remains a valuable tool for the reduction of anxiety among general populations, but is not recommended for use among children who have an autism spectrum disorder diagnosis. According to this study, the introduction of bergamot essential oil in a medical provider’s office may increase the subjective feelings of anxiety among children on the autism spectrum. While there remains potential for aromatherapy to have a positive effect on anxiety levels among children who have an autism spectrum disorder diagnosis, the specific oil(s) which may be recommended for use and the potential applications remain undiscovered. Further research is recommended to identify ways in which essential oils may improve quality of life for children on the autism spectrum.
REFERENCES


APPENDICES
APPENDIX A: IRB APPROVAL LETTER

Institutional Review Board Office of Compliance Middle Tennessee State University

and be aware that you may not receive a separate reminder to complete your continuing reviews. Failure in obtaining an approval for continuation will automatically result in cancellation of this protocol. Moreover, the completion of this study MUST be notified to the Office of Compliance by filing a final report in order to close-out the protocol.

Continuing Review Schedule:

<table>
<thead>
<tr>
<th>Reporting Period</th>
<th>Requisition Deadline</th>
<th>IRB Comments</th>
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<tbody>
<tr>
<td>First year report</td>
<td>9/30/2018</td>
<td>TO BE COMPLETED</td>
</tr>
<tr>
<td>Second year report</td>
<td>9/30/2019</td>
<td>TO BE COMPLETED</td>
</tr>
<tr>
<td>Final report</td>
<td>9/30/2020</td>
<td>TO BE COMPLETED</td>
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</table>

Post-approval Protocol Amendments:

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<tr>
<th>Date</th>
<th>Amendment(s)</th>
<th>IRB Comments</th>
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<tr>
<td>NONE</td>
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The investigator(s) indicated in this notification should read and abide by all of the post-approval conditions imposed with this approval. Refer to the post-approval guidelines posted in the MTSU IRB’s website. Any unanticipated harms to participants or adverse events must be reported to the Office of Compliance at (615) 494-8918 within 48 hours of the incident. Amendments to this protocol must be approved by the IRB. Inclusion of new researchers must also be approved by the Office of Compliance before they begin to work on the project.

All of the research-related records, which include signed consent forms, investigator information and other documents related to the study, must be retained by the PI or the faculty advisor (if the PI is a student) at the secure location mentioned in the protocol application. The data storage must be maintained for at least three (3) years after study completion. Subsequently, the researcher may destroy the data in a manner that maintains confidentiality and anonymity. IRB reserves the right to modify, change or cancel the terms of this letter without prior notice. Be advised that IRB also reserves the right to inspect or audit your records if needed.

Sincerely,
Institutional Review Board
Middle Tennessee State University

Quick Links:
Click here for a detailed list of the post-approval responsibilities. More information on expedited procedures can be found here.

This protocol can be continued for up to THREE years (10/31/2020) by obtaining a continuation approval prior to 10/31/2018. Refer to the following schedule to plan your annual project reports
APPENDIX B: INFORMED CONSENT DOCUMENTS

IRBF010a
RESEARCH WITH MINORS – PARENTAL PERMISSION
(Parental Consent form for Minors UNDER 12 years)

A.

PARENTAL PERMISSION
(Parents’ Copy)

Primary Investigator(s)   Jessie Hawkins, PhD Student
Contact information      Ms Hawkins phone 615-642-1919, jh6z@mtmail.mtsu.edu
Department Institution   Middle Tennessee State University
Faculty Advisor          Dr Norman Weatherby
Study Title              The effect of scent on anxiety scores among children with autism.
IRB ID                  18-2057 Expiration 10/31/2020
Arbitrary Tracking ID   (print)

The following information is provided to you because your child may qualify to participate in the above identified research study. Please read this disclosure document carefully and feel free to ask any questions before you agree to enroll your child. The researcher must adequately answer all of your questions before your child can be enrolled. The researcher MUST NOT enroll your child without an active consent from you. Also, a copy of this consent document, duly signed by the investigator, must be provided to you for future reference.

Your child’s participation in this research study is absolutely voluntary. You or your child can withdraw from this study at any time. In the event new information becomes available that may affect the risks or benefits associated with this research or your willingness to participate in it, you will be notified so that you can make an informed decision whether or not to continue your participation in this study.

For additional information about giving consent or your rights as a participant in this study, please feel free to contact the MTSU Office of Compliance (Tel 615-494-8918 or send your emails to irb_information@mtsu.edu. Please visit www.mtsu.edu/irb for general information and visit http://www.mtsu.edu/irb/FAQ/WorkinWithMinors.php for information on MTSU’s policies on research with children.

Please read this section and sign Section C if you wish to enroll your child. The researcher will not enroll your child without your physical signature.
1. Purpose of the study:
   Your child is being asked to participate in a research study because we are evaluating the effects of scent on the amount of anxiety a child experiences in the doctor's office.

2. General description of procedures to be followed and approximate duration of the study:
   The MTSU’s classification of this study is
   - Educational Tests – Study involves either standard or novel education practices which consists educational testing and such studies expose the minors to lower than minimal risk
   - Behavioral Evaluation – Although the study may or may not involve educational tests, the specific aim is to probe the child’s behavioral ability.
   - Physical Evaluation – The children will be asked to perform or part-take in physical activities or procedures. Examples of such studies simple physical exercises, medical or clinical intervention, pharmaceutical testing and etc. Due to the nature of these studies, your child may be exposed to more than minimal risk.

   This program is part of a research study and your participation is completely voluntary. You are free to withdraw at any time. In the event new research becomes available that may affect the risks or benefits associated with this research study or your willingness to participate in it, you will be notified so that you can make an informed decision whether or not to continue your participation in this study.

   We want to evaluate exposures to scent in exam rooms and to learn how to improve the overall experiences of children with autism during medical office visits. You have the right not to respond to any questions that you do not want to answer.

   In addition to your child's usual checkup intake, including blood pressure and heart rate, you will be provided a 20 question survey for your child to complete at the start of the checkup. This survey evaluates how your child feels in this exact moment. Please help them answer the questions reflecting their feelings at that exact moment in time, which may or may not reflect how they usually feel.

   After you have completed the survey, your child will proceed with his or her usual visit, either with or without a discernible scent in the exam room. After your 15 minute visit, you will again be provided with a 20 question survey to complete with your child. This should also be answered to reflect the way your child feels in that exact moment. Your child's blood pressure and heart rate will be taken again. At that point the visit will continue as it normally would, or if it has concluded, you will be provided contact information for the researcher should you have any questions. Completion of each survey will take 5-10 minutes.

3. What are we planning to do to your child in this study?
   In this study, your child will be asked 20 questions about the way he or she feels right now during the office visit. This will happen at the start of the visit and again after 15 minutes have passed. This information will be provided to the researcher, along with your child's age, sex, diagnoses, insurance type, blood pressure, and heart rate.

4. What will your child be asked to do in this study?
   Your child will be asked to answer the questions in the survey based on how he or she feels in that exact moment. This survey will take 5-10 minutes to complete.

5. What are we planning to do with the data collected using your child?
   The medical records of the child's data, including the scent that is in the examining room, will be analyzed to determine how scents in the doctor's office help or do not
help with overall anxiety. No personal identification information about you or your child will be included in the data. Your child will be identified by a research participant number and all data will be stored securely.

6. **What are your expected costs, effort and time commitment:**
   Participation in this study will not cost you anything. It may increase the total amount of time you are in the examining room while your child is completing the survey.

7. **What are the potential discomforts, inconveniences, and/or possible risks that can be reasonably expected as a result of participation in this study:**
   For the Child: Your child will be asked 20 questions about how he or she feels right now. These questions will be asked twice, once right away and again after the checkup.
   For you the Parent: You may need to help your child read or understand the questions in the survey. It is important that your child answers them based on how he or she feels in that exact moment, rather than overall.

8. **How will you or your child be compensated for enrolling in this study?**
   This study does not offer financial compensation.

9. **What are the anticipated benefits from this study?**
   This study provides valuable information about the impact of an aroma intervention for children with autism. Upon its conclusion, researchers and care providers will be able to better understand how children with autism respond to inhaled plant-based substances and how such interventions may improve overall quality of life for parents and children.

10. **Are there any alternatives to this study such that you or/and your child could receive the same benefits?**
    There are no known alternatives to this study which provide the same benefit.

11. **Will you or/and your child be compensated for study-related injuries?**
    This study is extremely safe and the aromatic oil is prepared in child-proof preparations. No compensation is provided if there are any study-related injuries.

12. **Circumstances under which the Principal Investigator may withdraw your child from study participation:**
    If you state that you or your child no longer wish to participate.

13. **What happens if you choose to withdraw from study participation?**
    If you withdraw from the study, you will be able to discontinue the survey. Nothing else will be asked of you. There is no penalty.

14. **Can you or/and your child stop the participation any time after initially agreeing to give consent/assent?**
    You and/or your child can discontinue the study at any time.
15. **Contact Information.** If you should have any questions about this research study or possibly injury, please feel free to contact Jessie Hawkins by telephone 615-642-1919 or by email jh6z@mtmail.mtsu.edu OR my faculty advisor, Dr. Norman Weatherby, at norman.weatherby@mtsu.edu.

16. **Confidentiality.** All efforts, within reason, will be made to keep the personal information in your child’s research record private but total privacy cannot be promised. Your information may be shared with MTSU or the government, such as the Middle Tennessee State University Institutional Review Board, Federal Government Office for Human Research Protections, *if* you or someone else is in danger or if we are required to do so by law.

Consent obtained by:

<table>
<thead>
<tr>
<th>Date</th>
<th>Researcher’s Signature</th>
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<table>
<thead>
<tr>
<th>Researcher’s Name and Title</th>
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</table>
B. Signature Section
(Researchers’ Copy)

Primary Investigator(s)  Jessie Hawkins  Student
Contact information  Ms Hawkins 615-642-1919 or jh6z@mtmail.mtsu.edu
Department Institution  Middle Tennessee State University
Faculty Advisor  Dr. Norman Weatherby  Department Health and Human Performance
Study Title  The effect of scent on anxiety scores among children with autism.
IRB ID  18-2057  Expiration 10/31/2020
Arbitrary Tracking ID  (print)

RESEARCHER SECTION

(This section will be signed by the researchers AFTER the parent signs in the bottom and returns this form in the stamped self-addressed envelope)

Parental Consent obtained by:

Date  PI’s Signature  PI’s Name & Title

Faculty Verification:

Date  Faculty Signature Print Name & Title

PARENT SECTION

The parent who agrees to enroll his/her child will sign this document and return only this page back to the researcher in the stamped self-addressed envelope provided by the researcher

No  Yes  I have read this informed consent document pertaining to the above identified research
No  Yes  The research procedures to be conducted have been explained to me verbally
No  Yes  I understand each part of the interventions and all my questions have been answered
No  Yes  I am aware of the potential risks of the study

By signing below, I give permission for my child, whose name is identified above, to participate in this study. I understand I can withdraw my child from this study at any time without facing any consequences.
The following section will be removed and destroyed to protect the participants.

PARENT’S SIGNATURE

__________________________ ________________________________
Date Signature of the Parent
APPENDIX C: STATE TRAIT ANXIETY INVENTORY FOR CHILDREN

1. I feel ........................................
   □ very calm □ calm □ not calm
   □ very upset □ upset □ not upset

2. I feel ........................................
   □ very pleasant □ pleasant □ not pleasant
   □ very nervous □ nervous □ not nervous

3. I feel ........................................
   □ very jittery □ jittery □ not jittery
   □ very rested □ rested □ not rested

4. I feel ........................................
   □ very scared □ scared □ not scared
   □ very relaxed □ relaxed □ not relaxed

5. I feel ........................................
   □ very worried □ worried □ not worried
   □ very satisfied □ satisfied □ not satisfied

6. I feel ........................................
   □ very frightened □ frightened □ not frightened
   □ very happy □ happy □ not happy

7. I feel ........................................
   □ very sure □ sure □ not sure
   □ very good □ good □ not good

8. I feel ........................................
   □ very troubled □ troubled □ not troubled
   □ very bothered □ bothered □ not bothered

9. I feel ........................................
   □ very nice □ nice □ not nice
   □ very terrified □ terrified □ not terrified

10. I feel ........................................
    □ very mixed-up □ mixed-up □ not mixed-up
    □ very cheerful □ cheerful □ not cheerful
APPENDIX D: BERGAMOT ESSENTIAL OIL GC ANALYSIS

BETA-PINENE 5.777
ALPHA-THUJENE 0.180
ALPHA-PINENE 1.068
CAMPHEME 0.025
SABINENE 0.968
MYRCENE 1.085
OCTANAL + ALPHA-PHELLANDRENE 0.065
ALPHA-TERPINENE 0.096
PARA-CYMENE 0.228
LIMONENE * 38.637
GAMMA-TERPINENE 7.147
EUCALYPTOL 0.160
(Z)-BETA-OCIMENE 0.046
(E)-BETA-OCIMENE 0.198
TERPINOLENE 0.301
LINALOL * 7.613
ACETATE DE LINALYLYE 31.512
ACETATE D’ALPHA-TERPENYLE 0.312
ACETATE DE NERYLE 0.662
ACETATE DE GERANYLE 0.527
GERANIAL * 0.292
BETA-BISABOLENE 0.303
BETA-CARYOPHYLLENE 0.243
ALPHA-TRANS-BERGAMOTENE 0.209
ACETATE D’OCTYLE 0.176
DECANAL 0.057
ALPHA-TERPINEOL 0.074
TERPINENE-4-OL 0.018
NERAL 0.185
CITROPTENE 0.075
BERGAPTENE 0.125

Total 98.364