PEDIATRIC AUTOIMMUNE NEUROPSYCHIATRIC DISORDER ASSOCIATED WITH STREPTOCOCCAL INFECTION (PANDAS): A QUALITATIVE STUDY OF PARENTAL PERCEPTIONS OF FACTORS IN REMISSION

by

Janice Weddle

Liberty University

A Dissertation Presented in Partial Fulfillment

of the Requirements for the Degree

Doctor of Philosophy

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Abstract

Pediatric autoimmune neuropsychiatric disorder associated with streptococcal infection (PANDAS) starts as the child's body has an inappropriate reaction to the immune response for streptococcal infection. PANDAS is characterized by the sudden onset of neuropsychiatric disorders, including obsessive-compulsive disorder (OCD), anxiety, chorea movements, and tics. Previous research has drawn conflicting conclusions on PANDAS treatment efficacy and long-term treatment outcomes leaving remission rates unclear. The purpose of this qualitative phenomenological case study was to explore parents' perceptions of factors related to PANDAS remission. Parents of children diagnosed with PANDAS were recruited through Facebook PANDAS support groups and the National Institute of Mental Health Outreach Partnership Program Aspire PANS/PANDAS newsletter and followed a link to a Qualtrics survey containing 16 questions related to perception of remission. Inclusion criteria included diagnosis of PANDAS from a medical doctor and being the legal parent or guardian of the PANDAS patient. No significant relationship was found between presence of remission and age or symptom severity. The average length of time of illness before receiving PANDAS diagnosis and treatment was 23.75 months, but length of illness before treatment was not related to presence of remission. The greatest healing effect for PANDAS symptoms was antibiotics; however, 85% of children in remission still had symptoms. This study sets a foundation for future studies to explore why and how various treatments are more or less effective, serves as a starting point for future experimental studies on treatment methods, and serves as a roadmap for families with a PANDAS diagnosis.

Key Words: *PANDAS, streptococcal infection, neuropsychiatric, autoimmune, remission*

Dedication

I have to thank my husband first, for not only supporting but encouraging me as a full-time student. I don't know many people that would support a partner beginning a doctoral program with two little kids and a full-time job during a pandemic, but without your support the dream of this degree would have been even harder to accomplish. I spent several years praying for the life I have today, and I have you to appreciate for that. Our marriage is the perfect testament to answered prayers and beauty for ashes. I think we provide the perfect balance to each other and are exactly what the other needs. I am so grateful to you through this process but so glad to be closing this chapter and as you know, when we are done with something, we are done with it.

My precious baby bear and sweet baby nugget, being a lifetime student has taught me many lessons, but the most important things I have learned about life have come from being your mom. I hope at the end of every day you know how incredibly loved you are and how deeply proud I am of you. Earning this degree is a huge accomplishment that I hope helps me shape scientific advancements, and even so, my greatest contribution to the world will always be the two of you.

To my parents that instilled in me a love of learning. It is hard to explain the appreciation for the two people that are the foundation to it all. You made sure I was afforded every opportunity to be happy and successful. You have not only given me a great life, but make sure my kids have all they could want and need, too. As an only child I definitely had all the attention, but had it not been for that, along with a small inherited competitive streak, who knows how things would have ended up. It is your love and

sacrifice that shapes my entire view of the world. You have supported me through everything and I only wish that everyone got to have parents as good as mine.

To my family, friends, and colleagues over the last two years as I've went through this process, I appreciate the support, patience, and understanding. Everyone around me sacrificed when school had to take the place of free time and other priorities, and the support of those close to me through this process is so very appreciated.

This better be where the fun starts.

Acknowledgments

My deepest appreciation goes to my wonderful dissertation committee, Dr. Laura Rolen and Dr. Kelly Gorbett. They have been the most encouraging and supportive committee that anyone could wish for. They have helped me through this process with patience, understanding, and have pushed and encouraged me to do my best work. I am eternally grateful for the time and effort they spent with me through this process.

I am grateful for the doctoral program at Liberty University. Had it not been for this program and PSYC 750 Biological Bases of Behavior, I don't know if I would have ever stumbled upon PANDAS, a diagnosis that saved my little bear. I pulled out my neuroscience book to look at effects of sleep deprivation, thanks to nug, and opened to a page on OCD. This led me to investigate sudden onset OCD in children which led me to PANDAS. This one moment in time has forever changed the life of everyone in my family.

To the participants in this study, thank you for your time and sharing your story with me to guide research to help our children. To the parents and kids who have missed out on their precious childhood, our children are warriors. PANDAS has given them all the superpowers of creative problem solving and empathy. Through their diagnosis they must use creative problem solving to make it through their struggles each day, and have learned only the purest empathy and humility that will serve them their entire lives. PANDAS kids know how it feels to be treated differently or be silently struggling inside; they will in turn take care to treat others with respect and without judgement. To all the kids who went before, allowed experimental treatments to be done, or are even still

undiagnosed or misdiagnosed, the PANDAS kids of the future will be standing on the shoulders of giants.

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CHAPTER 1: INTRODUCTION TO THE STUDY

Pediatric autoimmune neuropsychiatric disorder associated with streptococcal infection (PANDAS) was first described by Dr. Susan Swedo in 1998. PANDAS starts as the child's body has an inappropriate reaction to the immune response for streptococcal infection. PANDAS is characterized by the sudden onset of neuropsychiatric disorders, including obsessive-compulsive disorder (OCD), anxiety, chorea movements, and tics. There is now an accepted diagnostic and treatment framework for PANDAS, but long-term treatment outcomes and remission rates are still unclear. Previous research has drawn conflicting conclusions on PANDAS treatment efficacy. This study is a survey of parents' perceptions of PANDAS remission. The purpose of this qualitative phenomenological study was to explore parents' perceptions of factors related to PANDAS remission.

Background

PANDAS Overview

In 1998, Dr. Susan Swedo discovered a link similar to that of Rheumatic Fever and Sydenham Chorea, now known as Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections (PANDAS). PANDAS is a subset of Pediatric Acute-Onset Neuropsychiatric Syndrome (PANS). The distinction between PANS and PANDAS is the relationship with the disorder to Group A streptococcus infection. In PANDAS, there is a relationship between symptom onset and streptococcal infection. PANDAS is encephalopathy caused by an autoimmune disorder (Cooperstock et al., 2017).

PANDAS starts as the child's body has an inappropriate reaction to the immune response for streptococcal infection (Blackburn & Wang, 2020; Frick & Pittenger, 2016; Leonard & Swedo, 2001; Mink, 2016; Nave et al., 2018; Stagi et al., 2018; Williams et al., 2019; Williams et al., 2016;). PANDAS Network estimates that this disorder affects 1 in 200 children; however, it is believed many more children are affected but have been misdiagnosed (Dean et al., 2017; Leon et al., 2018).

PANDAS is characterized by the sudden onset of neuropsychiatric disorders, including obsessive-compulsive disorder (OCD), anxiety, and tics (Frick & Pittenger, 2016; Leon et al., 2018; Mink, 2016; Sigra et al., 2018; Stagi et al., 2018). Basal ganglia inflammation is a result of the body's misguided immune response to infectious triggers; in the case of PANDAS, it is a misguided response to the Group A streptococcal infection. The effects of basal ganglia inflammation can include many neuropsychiatric symptoms that resemble other illnesses, making many children go misdiagnosed. There are many disorders and/or syndromes that resemble PANDAS. Further studies are needed to determine the association and the biological pathways that connect streptococcal infection, autoimmune response, and the later development of behavioral disorders (NIH, 2021; Williams et al., 2016).

PANDAS Symptoms

PANDAS is characterized by the sudden onset of neuropsychiatric disorders, including obsessive-compulsive disorder (OCD), anxiety, and tics (Frick & Pittenger, 2016; Leon et al., 2018; Mink, 2016; Sigra et al., 2018; Stagi et al., 2018). Practitioners have developed a diagnostic framework tool that explains whether symptoms are categorized as mild, moderate, or severe (PPN, 2021). Basal ganglia inflammation is a

result of the body's misguided immune response to infectious triggers; in the case of PANDAS, it is a misguided response to the Group A streptococcal infection. The effects of basal ganglia inflammation can include many neuropsychiatric symptoms. See Table 1.

Table 1

Effects of Basal Ganglia Inflammation

Basal Ganglia is a relay station through which neurons that control:	**Inflammation may cause:**
Mood and Emotion	OCD, Mood Lability, Anxiety, Separation Anxiety
Behavior	OCD, Rage, Developmental Regression
Procedural Learning	Dysgraphia, Clumsiness, Decline in motor skills
Motor Movements	Tics, Choreiform Movements, Hypotonia
Cognition	Slow Processing Speed, Memory Issues, Decline in Cognitive Abilities, Decline in Mathematics Ability, Sensory Learning Deficits
Sensory	Sensitivity to light, sounds, smells, tastes, textures, clothing

The current working hypothesis regarding the pathophysiology of PANDAS is that a Group A Streptococcal infection takes place in a susceptible host, that then creates

the production of antibodies to the Group A Streptococcal infection. The GAS antibodies then cross-react with the cellular components of the basal ganglia (Blackburn & Wang, 2020; Dean et al., 2017; Frick & Pittenger, 2016; Nave et al., 2018; Snider & Swedo, 2004). In particular, these antibodies cross create in the caudate, nucleus, and putamen (Blackburn & Wang, 2020; Dean et al., 2017; Frick & Pittenger, 2016; Snider & Swedo, 2004). The OCD, tics, and accompanying neuropsychiatric symptoms in children with PANDAS arise as a result of the interaction of these antibodies and the neurons of the basal ganglia (Blackburn & Wang, 2020; Dean et al., 2017; Frick & Pittenger, 2016; Snider & Swedo, 2004).

Results from Geidd et al. (2000) show that there are participants with OCD and tics who show enlarged basal ganglia in MRI assessment. Recent discoveries with the T-Helper 17 (Th17) lymphocytes show these cells drive neuronal deficits in mice in postinfectious autoimmune encephalitis (Platt et al., 2020; Lotan et al., 2014). Basal ganglia encephalitis, which represents the subset of PANDAS, is triggered by the Th17 cells causing blood brain barrier breakdown, therefore letting in autoantibodies, leading to the neuropsychiatric symptoms associated with PANDAS (Dean et al., 2017; Platt et al., 2020).

In recent research, studies are attempting to identify genetic markers and etiology that could help diagnose PANDAS. Scientists have discovered the T-helper 17 (Th17) cell, which is a T-cell subset that produces interleukin-17 (IL-17) (Harabuchi & Takahara., 2019; Pilli et al., 2017; Platt et al., 2020; Tesmer et al., 2008). IL-17 is an extremely inflammatory cytokine (Tesmer et al., 2008). Research is finding in both human and mice studies that Th17 cells play an important role in the etiology of a group

of immune-mediated diseases that include psoriasis, rheumatoid arthritis, multiple sclerosis, inflammatory bowel disease, and asthma (Lotan et al., 2014; Tesmer et al., 2008). Research findings from Platt et al. (2020) demonstrate that the Th17 cells play a critical role in the entry of autoantibodies into the central nervous system and the Th17 cells create the pathogenesis to impair the central nervous system functions in encephalitis syndromes (Frick & Pittenger, 2016; Lotan et al., 2014; Williams et al., 2016).

PANDAS Treatments

Common PANDAS treatments recommended by the PANDAS Physicians Network (PPN) protocol include adenotonsillectomy, antibiotics, corticosteroids, plasmapheresis, cognitive behavioral therapy, and intravenous immunoglobulin (IVIG) (Alexander et al., 2011; Ayaydin & Abali, 2010; Barzman et al., 2018; Brown et al., 2017; Calaprice et al., 2018; Demesh et al., 2015; Kovacevic et al., 2015).

In the study by Prasad et al. (2021), researchers investigated which treatments would be most effective and satisfactory for treating PANDAS. In the study by Prasad et al., (2021), subjects were most commonly treated with antibiotics (n=60). Tonsillectomy was the second most occurring treatment (n=50), then IVIG (n=24), then prescription Rituximab (n=9), steroids (n=12), and plasma exchange (n=6). In a longitudinal study of PANDAS treatment outcomes by Leon et al., (2018), a double-blind, placebo-control study of 35 children who received IVIG were followed for a mean of 3.3 years and received a variety of treatments such as antibiotics, IVIG, psychiatric medications, cognitive behavioral therapy, or a combination.

Because PANDAS was first discovered in 1998, long-term treatment outcomes for PANDAS patients remains unknown or inconclusive due to lack of double-blind placebo-controlled studies (Alexander et al., 2011; Ayaydin & Abali, 2010; Barzman et al., 2018; Brown et al., 2017; Calaprice et al., 2018; Dean et al., 2017; Kovacevic et al., 2015; Leon et al., 2018; Mink et al., 2016; Nave et al., 2018; Stagi et al., 2018; Williams et al., 2016; Williams et al., 2019). Many PANDAS patients undergo a variety of treatment methods (Hesselmark & Bejerot, 2019); therefore, conducting a study on parents' perspectives on treatments along with exploring factors in remission, such as how age and length of illness relate to remission rate, was the focus of this study in order to serve practitioners and families through future research investigating how to best treat PANDAS.

Problem Statement

Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcal Infection (PANDAS) is an autoimmune disorder that is a result of the body's misguided immune response to streptococcal infection (Frick & Pittenger, 2016; Leon et al., 2018; Mink, 2016; Sigra et al., 2018; Stagi et al., 2018). PANDAS is characterized by the sudden onset of neuropsychiatric disorders, including obsessive-compulsive disorder (OCD), anxiety, tics, and chorea movements (Frick & Pittenger, 2016; Leon et al., 2018; Mink, 2016; Sigra et al., 2018; Stagi et al., 2018). PANDAS was first discovered by Dr. Susan Swedo in 1998, therefore long-term treatment efficacy remains unclear. Many PANDAS patients undergo a variety of treatment methods in order to reach remission (Calaprice et al., 2018; Hesselmark & Bejerot, 2019). Previous research has drawn conflicting conclusions on PANDAS treatment efficacy (Ayaydin & Abali, 2010;

Barzman et al., 2018; Brown et al., 2017; Calaprice et al., 2018; Cooperstock et al., 2017; Demesh et al., 2015; Dop et al., 2021; Fusco et al., 2010; Kovacevic et al., 2015; Leon et al., 2018; Lepri et al., 2019; Mink, 2016; Nave et al., 2018; Prasad et al., 2021; Rajgor et al., 2018; Sigra et al., 2018; Spartz et al., 2017; Williams et al., 2016). This study investigated parents' perceptions on factors of remission in PANDAS. This study used a qualitative design to gain understanding of the PANDAS remission experience, which will lead to areas for future research to expand on areas of significance in factors of remission in PANDAS.

A study by Calaprice et al. (2018) retrospectively examined long-term outcomes of PANS/PANDAS. However, this study did not separate PANS/PANDAS and investigated caregiver reported treatment efficacy, but did not address symptom exacerbations or maintenance over time. Cooperstock et al. (2017) explains that symptom exacerbations are common, but does not further explain how frequent or long-lasting these exacerbations are. A study by Colvin et al. (2021) states that the cognitive, graphomotor, and psychosocial challenges in PANDAS patients can be ongoing even if the patient is not currently experiencing a symptom exacerbation. Studies by Latimer et al. (2015) and Gruijter et al. (2021) suggest that length of illness and age could be related to remission; however, both concluded these findings need further investigating. Cross et al. (2021) states that at 31 months post-treatment, patients reached complete remission. However, this study does not definitively state the journey or details of remission or remission maintenance. Studies related to treatments leading to remission, the length of time reaching remission takes, and other factors of remission such as age and length of illness, are scarce.

This study investigated parents' perceptions on factors of remission in PANDAS. This study examined patterns related to age, severity of illness, treatment methods, and symptom exacerbations as factors of remission in PANDAS. Studies related to long-term outcomes of PANDAS, effective treatments, and remission management are scarce and/or inconclusive. This study was conducted to discover patterns leading to remission and guide future research on exploration of factors of remission in PANDAS in addition to serving as a road map for parents of children recently diagnosed with PANDAS.

Purpose of the Study

The purpose of this qualitative phenomenological case study was to explore parents' perceptions of factors contributing to the remission of PANDAS. This study aimed to discover patterns in reaching PANDAS remission related to age, severity of illness, treatment methods, and symptom exacerbations. The study used a 16-question original survey on Qualtrics related to parents' perceptions of factors of remission in PANDAS. Findings from this study can be used in future research to discover cause and effect relationships between treatment methods, age, and symptom severity to better guide treatment protocols in the future.

Research Questions

RQ1: According to parents' perceptions, which treatment is most effective in achieving remission?

RQ2: According to parents' perceptions, how long does achieving remission take?

RQ3: According to parents' perceptions, is length of PANDAS illness prior to receiving diagnosis and treatment related to achieving remission?

RQ4: According to parents' perceptions, is severity of PANDAS symptoms related to achieving remission?

RQ5: According to parents' perceptions, is age of PANDAS patient at symptom onset related to achieving remission?

RQ6: According to parents' perceptions, is presence of puberty related to PANDAS symptoms?

RQ7: According to parents' perceptions, are symptom flares experienced after achieving remission?

RQ8: According to parents' perceptions, is gender related to presence of remission?

RQ9: According to parents' perceptions, what is the most effective treatment for remission maintenance?

Assumptions and Limitations of the Study

Limitations of this study are the parents' perceptions, whether it is mother or father completing the survey, as mothers and fathers could have different perceptions of the PANDAS experience. In a study by Calaprice et al. (2018), 95% of surveys were completed by mothers, 4% by fathers, and <1% other. Another limitation could be recall bias, as parents may not clearly remember lengths of time or symptom severity. More possible limitations could be conservatism, regressive bias, or consistency bias, as parents may not remember exactly how severe the PANDAS symptoms were or the effectiveness of various treatments at a particular time. A limitation of this study is that it did not address specific brands, doses, or length of time various treatments were used. A

delimitation of this study is not verifying the diagnosis of PANDAS through medical records.

A challenge of the study was the potential varying perceptions of the definition of remission. Studies examining remission in lupus and rheumatoid arthritis discuss the varying definitions of remission, such as defining remission as either no clinical sign of disease or remission on treatment (Felson, 2011; Wilhelm et al., 2016). Another challenge was the vast number of potential treatments that could lead to remission, as many PANDAS patients use more than one treatment (Hesselmark & Bejerot, 2019).

Theoretical Foundations of the Study

The goal of this study was to better understand the factors involved in remission for PANDAS patients according to parents' perceptions. Rallis and Rossman (2012, p. 18) state that the goal of qualitative research is learning by transforming data into information that can be used. Therefore, this research is best suited for a qualitative study to allow for the understanding of the lived experience of PANDAS families in remission rather than quantitative research testing hypotheses since no studies on PANDAS remission could be located. According to Creswell and Poth (2018, p. 8), qualitative research begins with an assumption and uses interpretive and theoretical frameworks to inform the study to address research problems by addressing a group with a human problem, in this case, PANDAS remission. In order to study the problem, the researcher takes a qualitative approach in order to find patterns or themes. The findings of the study include a complex description and interpretation of the problem and its contribution to the literature (Cresswell & Poth, 2018, p. 8). Mack et al., (2005) describes qualitative

research as seeking to explore phenomena using more flexible instruments in order to describe and explain relationships.

Phenomenology

According to Cresswell and Poth (2018), phenomenology has an emphasis on a single concept or idea; in this study, this concept is remission. This study aimed to understand parents' perceptions of factors of remission from parents of children diagnosed with PANDAS. As a methodological approach, phenomenology allows for the examination of the lived experience of the journey to remission in PANDAS. Hardy (2018, p. 20) describes phenomenology as understanding experiences as people live through situations and experiences. The researcher's role is to attempt to discover and understand these lived experiences and transform the data that is collected into information that can be useful. Using a pragmatism paradigm, the aim of this study was to understand the experiences that can lead to solving problems. This study could be the first of many to explore remission experiences in PANDAS that can solve issues related to treatments and reaching remission.

There are two types of phenomenology, Hermeneutic and transcendental (Cresswell & Poth, 2018). This study used transcendental phenomenology, which is oriented toward the description of the experience of the participants. The researcher uses the concept of epoche in order set aside their own experiences. The researcher bracketed herself out of the study by understanding her own relationship with PANDAS and will allow these experiences to be set aside so that the focus is on the experience of the participants. Transcendental phenomenology allows the researcher to analyze the data by reducing the information to significant statements that can be generalized into patterns or

themes. Upon finding these themes and patterns, the researcher is able to provide a textural description of the experience. The description of their experience, known as the structural description, describes how the phenomenon was experienced in relation to conditions, situations, or context. In this study, the phenomenon is remission, with trying to gain understanding on how remission is related to other conditions such as age, length of illness, and severity of illness.

In a phenomenological approach, the researcher moves between etic and emic perspectives (Hardy, 2018). Hardy (2018) describes etic as the outsider's perspective, and it is achieved by examining and interpreting data through a psychological lens in which the researcher finds helpful to bring an understanding of the research questions. Hardy (2018) describes emic as the insider's perspective, which takes a pragmatic approach to help the researcher shape the varied nature of the explanations from the study. Using epoche to bracket the researcher's personal experiences out of this study, the emic can help the researcher focus on results of the study by interpreting the varied and provisional nature of the findings. The pragmatism paradigm asserts that the best method is one that solves problems. This concept allows the researcher to translate the lived experiences of remission in PANDAS families into information that can be used to guide future research on treatment methods and remission outcomes. The transcendental phenomenological approach allows for flexibility in the study so that the researcher can modify guidelines to fit their research objectives (Creswell & Poth, 2018). The flexibility of this method is useful in this study as the researcher had to create an original survey for this study since no previous research could be found. There is also not enough literature that could be located that could be used to develop hypotheses related to reaching remission, which is

why the researcher chose this approach in order to create a starting point of research on PANDAS remission.

Data in this study were analyzed using a transcendental phenomenological approach. The intent of this approach in this study is that the researcher attempts to make sense of the phenomenon, remission, under investigation. Creswell and Poth (2018) describe phenomenology as describing the personal experiences with the phenomenon under study. The phenomenon seeking to be better understood in this study is the process of remission in PANDAS. Phenomenology creates a description of what the participants in the study experienced and how the experience happened, and it aims to capture the essence of the phenomenon (Creswell & Poth, 2018, p. 201). By using a transcendental phenomenological approach, the researcher is able to find themes and patterns in the phenomena under investigation. In a transcendental phenomenological case study, reality needs to be interpreted.

This study took a direct interpretation approach, which allowed the researcher to look at factors of remission in PANDAS and extrapolate the data in more meaningful ways (Cresswell & Poth, 2018, p. 206). Mack et al. (2005) notes that an advantage of qualitative research is the flexibility in data collection. This study used Wolcott's (1994) approach to validation with the premise that in this study validity of a survey tool would neither guide nor inform the qualitative research, as the goal is to gain a better understanding of PANDAS remission (Cresswell & Poth, 2018, p. 255). Wolcott (1994) states that understanding is better than validity, and the goal of this study is better understanding of PANDAS remission (Cresswell & Poth, 2018, p. 255).

Instruments used to measure remission in other diseases, such as systemic lupus erythematosus and rheumatoid arthritis have been developed. Remission can have several definitions depending on the patient and their experience. Some examples of various definitions of remission include clinical remission, complete remission, clinical remission on treatment, and complete remission on treatment (Wilhelm et al., 2016). In rheumatoid arthritis, the remission is typically measured using a cut off score on the disease activity score (DAS28) (Gul et al., 2021). To date, there is no validated instrument specifically for the measurement of PANDAS remission. Therefore, lack of definition of remission is a limitation of this study, as survey participants may describe remission differently. Balancing these approaches allowed for logical generalizations related to PANDAS remission to be analyzed to contribute to areas of need in future research.

Biblical Foundations of the Study

The aim of this study was to gain parents' perceptions of PANDAS remission, so that this study could provide hope for parents currently battling PANDAS and provide them with information to help them persevere. The love of a parent for their child keeps them hoping for remission and helping their child in any way they can. The Bible states the importance of hope and love in 1 Corinthians 13:13, "Now these three remain, faith, hope, and love, but the greatest of these is love." A parent's love for their child encourages them to press on during difficult times of illness. Proverbs 24:16 says, "Though a righteous man falls seven times, he rises again." As the illness typically takes time to heal and many periods without worldly support or answers, Ephesians 6:11-12 says, "Put on the whole armor of God, that you may be able to stand against the schemes of the devil. For we do not wrestle against flesh and blood, but against the rulers, against

the authorities, against the cosmic powers over this present darkness, against the spiritual forces of evil in the heavenly places." Literature on remission is scarce and inconclusive. PANDAS parents do not know what they are up against or for how long when receiving a PANDAS diagnosis. In regard to keeping hope and persevering on the road to remission, the Bible tells us in John 16:33, "I have told you these things, so that in me you may have peace. In this world you will have trouble. But take heart! I have overcome the world."

During times of uncertainty when dealing with a PANDAS diagnosis of a child, parents must equip themselves with the armor of God to persevere through the disorder to reach remission. In 2 Corinthians, Paul prays to have the thorn from his flesh removed on three different occasions, but God does not remove it and explains that it is beneficial to him. 2 Corinthians 12:7-9 states, "To keep me from becoming conceited because of these surpassingly great revelations, there was given me a thorn in my flesh, a messenger of Satan, to torment me. Three times I pleaded with the Lord to take it away from me. But he said to me, 'My grace is sufficient for you, for my power is made perfect in weakness.' Therefore, I will boast all the more gladly about my weaknesses, so that Christ's power may rest on me." Parents must keep in mind in dealing with this illness that His power is made perfect in our weakness, such as the weakness of a child with an illness. Parents have to persevere for the sake of their children. As parents hope faithfully for remission, they can take comfort in God's promises and eventual healing. Deuteronomy provides an example that although the family may be in a current uncomfortable place, it is not permanent. With God all things are possible, including remission. Parents keep hope that one day their child will no longer be battling this illness. Deuteronomy 1:6 says, "You have been at this mountain long enough. It is time to

move on." Although parents are rightfully discouraged, they must remember to put their faith in God and wait for His timing for healing. Hebrews 12:1 says, "And let us run with perseverance the race marked out for us."

Definition of Terms

The following is a list of definitions of terms that are used in this study.

Adenotonsillectomy– Surgical removal of the tonsils and adenoids (Demesh, 2015).

Antigen- a toxin or other foreign substance that induces an immune response in the body to create antibodies (Rose & Mackay, 2006).

Autoimmune- A disease in which the body's immune system mistakes its own healthy tissues as foreign and attacks them, whether directed against foreign antigens or self-antigens (Rose & Mackay, 2006). Most autoimmune diseases cause inflammation (Rose & Mackay, 2006).

Chorea– Involuntary, ongoing, random-appearing sequences of movement (Yilmaz & Mink, 2019).

Dysgraphia- Learning disorder where writing skills are below expected level for age and/or cognitive level. Can include decline in handwriting abilities due to psychiatric issue and can include decline in handwriting readability and margin drift (Chung & Patel, 2015).

Flare- Worsening of PANDAS related symptoms and/or loss of function (Gromark et al., 2022).

IVIG– Intravenous Immunoglobulin (Kovacevic, 2015).

PANDAS– Pediatric autoimmune neuropsychiatric disorder associated with streptococcal infection (Swedo et al., 1998).

PANS- Pediatric autoimmune neuropsychiatric syndrome, PANDAS is a subset of PANS. PANS does not have a direct link to streptococcal infection as does PANDAS and can be brought on my many infections (Swedo et al., 2015).

Sequela- a long-term effect of a temporary disease or injury (Rose & Mackay, 2006).

Streptococcal Infection- Commonly known as "strep throat"

Tics– Sudden, rapid, recurrent motor movement tics, such as shrugging or neck twisting, or vocalization, such as throat clearing or coughing (Ueda & Black, 2021).

Significance of the Study

The results of this study allow for drawing introductory conclusions about remission, as the disorder is still new enough at the time of this study that the literature is lacking in long-term outcomes. It is not clear what type of remission is the goal in PANDAS, as remission could mean complete remission, clinical remission, complete remission on treatment, or clinical remission on treatment. As a parent, it is scary to not know what to expect regarding treatment and remission, therefore it was an aim of this study to provide hope and a road map for parents who have a child with this disorder. This study serves as a stepping stone for future research to be able to examine more closely how symptom severity, age, and length of illness can be further investigated to guide treatment plans to help children with PANDAS receive appropriate and curative treatments.

Summary

In 1998, Dr. Susan Swedo first described PANDAS as the association between Group A Streptococcal infection and neuropsychiatric disorders. The medical community has been slow to accept PANDAS as a diagnosis, regardless of families who can show

vast improvement and complete healing for the child through PANDAS treatment protocols. PANDAS Network estimates approximately 1 in 200 children suffer from PANDAS (Leonard & Swedo, 2001). This number is hard to estimate because it is believed so many children go misdiagnosed due to lack of practitioner knowledge on PANDAS. Future research should be aimed at creating practitioner and community awareness of PANDAS, exploring which treatment methods are most effective in reaching remission of PANDAS, and research on why some treatments are more effective than others and how to maintain remission.

CHAPTER 2: LITERATURE REVIEW

Introduction

PANDAS starts as the child's body has an inappropriate reaction to the immune response for streptococcal infection. Research by Snider and Swedo (2004) found a postinfectious autoimmune-mediated etiology for children with sudden onset of Obsessive-Compulsive Disorder (OCD) and tics. This reaction creates brain changes in the child, which leads to symptoms such as OCD, anxiety, tics, personality changes, decline in math and handwriting abilities, sensory sensitivities, restrictive eating, and more (Dean, et al., 2017; Frick & Pittenger, 2016; Leon et al., 2018; Mink, 2016; Sigra et al., 2018; Stagi et al., 2018). PANDAS Network estimates that this disorder affects 1 in 200 children, however many children are misdiagnosed. Most PANDAS research is based on the hypothesis that certain infections can trigger changes in both behavior and movement in children (Murphy et al., 2007). Many doctors who are not educated on PANDAS will diagnose the child with OCD, anxiety, Tourette Syndrome (TS), autism, or Attention-Deficit-Hyperactivity-Disorder (ADHD), rather than finding the issue creating the symptoms. This is an issue because the symptoms the child is presenting with are due to the inflammation of the brain and a result of an autoimmune response, and with proper treatment, the child will no longer have these neuropsychiatric disorders. In PANDAS, the autoimmune response triggers basal ganglia inflammation of the brain, which leads to the neuropsychiatric symptoms. In the 1980s, studies of children with Sydenham Chorea found that it could serve as a useful model of pathophysiology for childhood onset neuropsychiatric symptoms, which led to the development of PANDAS (Leonard & Swedo, 2001).

Basal ganglia inflammation is a result of the body's misguided immune response to infectious triggers; in the case of PANDAS, it is a misguided response to the Group A streptococcal infection. The effects of basal ganglia inflammation can include many neuropsychiatric symptoms.

Description of Research Strategy

Identification and Selection of Studies

The literature search was performed using the Jerry Falwell Library online database. Inclusion criteria were peer-reviewed journal articles in English of any date range, with 81% being published between 2015 and 2021. Searches were conducted in Spring 2021 and again in Fall of 2021, and primarily used key search terms *PANDAS, Pediatric Autoimmune, Streptococcal, Sydenham Chorea, autoimmune tonsillectomy, and autoimmune intravenous immunoglobulin.*

Identification and Selection of Biblical Study

Biblical word study was performed using Bible Gateway, Study Light, and Nave's Topical Bible Concordance Online. Word study searches were conducted using key search terms *persevere, perseverance, hope, and endurance.*

Review of Literature

PANDAS Overview

PANS/PANDAS is encephalopathy caused by an autoimmune disorder (Cooperstock et al., 2017). Encephalitis is severe inflammation of the brain that includes many possible causes and complex diagnosis (Li et al., 2021). Cooperstock et al., (2017) provides a consensus on management guidelines from PANS/PANDAS experts who gathered at the PANS/PANDAS consortium. At the consortium, the experts gathered to

create a much-needed guideline for diagnosis and treatment of children suffering from PANS/PANDAS. Both PANS and PANDAS are associated with the body's misguided response to infection (Sigra et al., 2018). Mora et al. (2020) states that childhood immune activation by both viral and bacterial infections may increase the risk of neuropsychiatric disorders. PANS/PANDAS is characterized by the sudden onset of neuropsychiatric disorders, including obsessive compulsive disorder (OCD), anxiety, and tics (Sigra et al., 2018). The most common infections that can lead to PANS/PANDAS include infections of the upper respiratory tract, which can include rhinitis, sinusitis, and pharyngitis (Cooperstock et al., 2017). The most common infection related to PANS/PANDAS is Group A Streptococcus (GAS). If the onset of symptoms is able to be linked to a GAS infection, the patient is diagnosed as PANDAS; if the onset of symptoms is unable to be linked to a GAS infection, the patient is diagnosed PANS. However, many infection types can trigger an immune response to onset or exacerbate symptoms, therefore, it is likely PANS/PANDAS nonspecific immune activation mechanisms contribute to the symptoms of PANS/PANDAS (Cooperstock et al, 2017).

PANDAS Etiology

Basal ganglia inflammation is a result of the body's misguided immune response to infectious triggers; in the case of PANDAS, it is a misguided response to the Group A streptococcal infection (Alexander et al., 2011; Ayaydin & Abali, 2010; Barzman et al., 2018; Brown et al., 2017; Bruijn et al., 2020; Calaprice et al., 2018; Dean et al., 2017; Kovacevic et al., 2015; Leon et al., 2018; Mink et al., 2016; Nave et al., 2018; Stagi et al., 2018; Williams et al., 2019; Williams et al., 2016). The effects of basal ganglia inflammation can include many neuropsychiatric symptoms that resemble other illnesses,

making many children go misdiagnosed (Goncalves et al., 2018). Further studies are needed to definitively describe the association and the biological pathways that connect streptococcal infection, autoimmune response, and the later development of behavioral disorders. The current working hypothesis regarding the pathophysiology is that a GAS infection takes place in a susceptible host, that then creates the production of antibodies to the GAS infection that then cross-react with the cellular components of the basal ganglia. The neuropsychiatric symptoms in children with PANDAS arise as a result of the interaction of these antibodies and the neurons of the basal ganglia (Dean, et al., 2017; Frick & Pittenger, 2016; Kovacevic et al., 2015; Leon et al., 2018; Mink, 2016; Sigra et al., 2018; Stagi et al., 2018).

The exact mechanism of pathogenesis of GAS related neuropsychiatric disorders has not been exclusively proven, but it is proposed that the autoimmune mechanism by antibodies against the GAS infection bind to different brain regions in the basal ganglia altering neurotransmission (Li et al., 2021; Mora et al., 2020; Xu et al., 2021). A study by Quagliariello et al. (2018) concludes that streptococcal infection can alter gut microbiota in children with PANDAS leading to a pro-inflammatory status through the selection of specific bacterial strains associated with gut inflammation and immune response activation.

Sydenham Chorea

In the 1980s, studies of children with Sydenham Chorea (SC) found that it could serve as a useful model of pathophysiology for childhood onset neuropsychiatric symptoms, which led to the development of PANDAS (Swedo, 1998). PANDAS has been conceptualized as a forme fruste of SC (Kovacevic et al., 2015; Swedo et al., 2015).

SC is a neurological disorder of childhood resulting from infection from GAS infection. SC is an autoimmune response to a variant of streptococcus, like PANDAS. SC is a subset of rheumatic fever. SC creates irregular and involuntary movements of the body, known as choreiform movements (Kovacevic et al., 2015; Williams & Swedo, 2015). Choreiform movements are also a symptom of PANS/PANDAS. The random choreiform movements with PANS/PANDAS and Sydenham Chorea are a result of the autoimmune response to the streptococcal bacteria resulting in inflammation of the basal ganglia of the brain.

Symptoms of SC are characterized by rapid, irregular, and involuntary movements of the arms and legs, trunk, and facial muscles known as chorea movements and may include: uncoordinated movements, muscular weakness, stumbling and falling, slurred speech, difficulty concentrating and writing, and emotional instability.

The symptoms of SC can vary from a halting gait and slight grimacing to involuntary movements that are frequent and severe enough to be incapacitating (Yilmaz & Mink, 2020). There is no specific treatment for SC. When the severity of movements interferes with rest, sedative drugs, such as barbiturates or benzodiazepines, may be needed (Yilmaz & Mink, 2020).

Most children will make a full recovery from SC, although a small number will continue to have disabling, persistent chorea despite treatment (Yilmaz & Mink, 2020). Doctors recommend that children who have had SC take penicillin over the course of 10 years to prevent additional manifestations of rheumatic fever (Yilmaz & Mink, 2020). A study by Fusco and Spagnoli (2018) found that corticosteroids were effective in both short and long-term treatment of SC. A study by Favaretto et al. (2020) concluded that

corticosteroid treatment was effective for SC. Treatment and research regarding rheumatic fever and SC has helped guide discovery and treatment of PANDAS.

PANDAS Pathogenesis

Li et al. (2021) states that recent studies have been successful at elucidating the causal relationship between autoimmune central nervous system diseases and infections. Li et al. (2021) describes the process of postinfectious autoimmune encephalitis as occurring in three stages: the infection activating the immune response, which leads to antibody production and tissue damage, then the injured tissue releases antigens that are taken up by antigen-presenting cells, which leads to the production of autoantibodies.

In recent research, studies are attempting to identify genetic markers and etiology that could help diagnose PANDAS. Scientists have discovered the T-helper 17 (Th17) cell, which is a T-cell subset that produces interleukin-17 (IL-17) (Tesmer et al., 2008). IL-17 is an extremely inflammatory cytokine (Tesmer et al., 2008). Research is finding in both human and mice studies that Th17 cells play an important role in the etiology of a group of immune-mediated diseases, that includes psoriasis, rheumatoid arthritis, multiple sclerosis, inflammatory bowel disease, and asthma (Tesmer et al., 2008). PANDAS is brought on as a response to streptococcal infection, and one of the areas of etiology is between the Th17 cell and Streptococcus Pneumoniae (Tesmer et al., 2008). Research findings from Platt et al., (2020) demonstrate that the Th17 cells play a critical role in the entry of autoantibodies into the central nervous system and the Th17 cells create the pathogenesis to impair the central nervous system functions in encephalitis syndromes, such as inflammation of the basal ganglia in PANDAS.

T-Helper 17 (Th17) Lymphocytes

Discoveries with the T-Helper 17 (Th17) lymphocytes show these cells drive neuronal deficits in mice in postinfectious autoimmune encephalitis (Platt et al., 2020; Xu et al., 2021). Th17 cells have been implicated in the brains of several central nervous system diseases, including multiple sclerosis, autism spectrum disorders, epilepsy, and Alzheimer's. Basal ganglia encephalitis, which represents the subset of PANDAS, is triggered by the Th17 cells causing blood brain barrier breakdown, therefore letting autoantibodies cross the blood-brain barrier, leading to the neuropsychiatric symptoms associated with PANDAS (Li et al., 2021; Mora et al., 2020; Platt et al., 2020; Xu et al., 2021). In mice with GAS infection, Th17 lymphocytes were activated and migrated from the nose to the brain (Li et al., 2021). These Th17 lymphocytes cause the breakdown of the blood brain barrier and allow the autoantibodies to enter the central nervous system (Li et al., 2021; Mora et al., 2020). Li et al. (2021, p.31) also states that, "The Th17 lymphocytes also activate microglia and impair neuronal circuits. Thus, Th17 lymphocytes are a potential target for the treatment of autoimmune encephalitis."

In preclinical animal models, the induction of PANDAS has been performed through injection of the GAS antigen (Mora et al., 2020). The immune effects of the GAS antigen or antibodies in the animal models increased the immunoglobulin IgG antibodies and immunoglobulin-like receptors in the serum plasma levels and within areas of the brain including the striatum, the thalamus, and the frontal cortex (Mora et al., 2020). In animal models, the behavioral assessment of animals exposed to GAS showed long-term changes in various aspects of behavior, including locomotion, cognition, and emotion

(Mora et al., 2020). Results from Geidd et al. (2000) show that there are subjects with OCD and tics that show enlarged basal ganglia in MRI assessment.

In a study by Rodriguez et al. (2019), patients with OCD had significantly higher levels of Th17 cells than healthy controls. The study by Rodriguez et al. (2019) also discovered that the levels of Th17 cells progressively increased with the duration and severity of OCD. The results of this study provide further evidence of the involvement of immune dysregulation in the pathophysiology of OCD. In a study by Gerentes et al. (2019), results showed that inflammation involving the immune system was observed in patients with OCD, suggesting that possible treatment of OCD could benefit from further studies targeting infection and inflammation as OCD treatment options. Platt et al., (2017) states that because the blood-brain barrier permeability is the avenue of autoimmune encephalitis, future treatment avenues could rely on modulating the blood-brain barrier using biological or chemical therapeutics such as reactivation of the signaling pathways that normally function to form the blood brain barrier during development, could be used to repair the dysfunctional barrier during disease.

There is still much to learn regarding the etiology of PANDAS. Further investigating the role of the Th17 cells contributions in the central nervous system autoimmunity diseases could help lead to the development of improved diagnostic tools which could lead to immunotherapeutic treatments that are targeted against T cells or their cytokines, that could be more effective than current treatment regimens (Li et al., 2021; Pilli et al., 2017).

Antibodies and Molecular Mimicry

The pathogenesis of acute rheumatic fever, rhematic heart disease, Sydenham Chorea, and other autoimmune sequelae is related to autoantibodies that are characteristic of autoimmune disease and result from the immune response to GAS (Chain et al., 2020; Cunningham, 2019; Kovacevic et al., 2015). PANDAS has been conceptualized as a forme fruste of Sydenham Chorea (Kovacevic et al., 2015). Using SC as a forme fruste to PANDAS is a way to attempt to understand the pathogenesis of PANDAS. The sharing of host and streptococcal epitopes leads to molecular mimicry between the streptococcal and the host antigens that are recognized by the autoantibodies during the host response (Bruijn et al., 2020; Cunningham, 2019; Kovacevic et al., 2015). When two antigens share an identical epitope or when two different epitopes have similar shapes or charges, it is possible for an antibody produced for one epitope to cross-react against the other the process of molecular mimicry (Chain et al., 2020; Cunningham, 2019; Dean et al., 2015). Cross-reactive antigens are molecules on the group A streptococcus that mimic host molecules and during infection or immunization induce an autoimmune response against host tissues leading to the autoimmune group A streptococcal sequelae (Cunningham, 2019). Molecular mimicry is used to describe the immunological cross-reactivity between the host and the bacterial antigens (Chain et al., 2020; Cunningham, 2019; Swedo et al., 2015). A study by Xu et al. (2021) discusses PANDAS resulting from the postinfectious production of antibodies that target the basal ganglia through the phenomenon of molecular mimicry. This hypothesis is drawn from the pathophysiology of Sydenham Chorea. Results from the study by Xu et al. (2021) finds that PANDAS serum IgG shows selectively elevated binding to cholinergic interneurons in mice striatum’s.

Immunological cross-reactions between streptococcal and host molecules have been identified by antibodies or T cells that react with streptococcal components and tissue antigens (Cunningham, 2019). In a study by Frick et al. (2018), antibodies in serum from children with PANDAS bound to ~80% of cholinergic interneurons, which was significantly higher than the only <50% of binding seen in healthy controls. Elevated binding to cholinergic interneurons resolved with symptom improvement after treatment with intravenous immunoglobulin (Frick et al., 2018). Antibody-mediated dysregulation of striatal cholinergic interneurons provides further information on the pathophysiology of PANDAS.

Genetic Considerations of PANDAS

GAS infection causes autoimmune sequelae in many target tissues, including tissues of the heart, kidneys, and central nervous system that manifest as acute rheumatic fever and Sydenham chorea, and PANDAS. It is hypothesized that predisposition to post-GAS autoimmunity has a genetic component since rhematic fever, Sydenham chorea, and PANDAS are all sex-skewed (Platt, 2019; Swedo et al., 2015). PANDAS is more prevalent in boys than girls at a rate of 3:1 (Calaprice et al., 2018; Platt, 2019). Platt (2019) states that genome wide association studies have implicated major histocompatibility class I and class II alleles in acute rheumatic fever, Sydenham Chorea, Autoimmune Encephalitis, and Acute Disseminated Encephalomyelitis. Platt (2019) states that genome wide association studies have demonstrated a genetic predisposition for recurrent childhood infections. A study by Jones et al. (2019, p.309) concluded that maternal autoimmunity can activate fetal microglia or alter transcription of neurodevelopment vulnerability or immune genes in utero, and it is, “an environmental

factor that increases the expression and severity of neurodevelopmental problems and susceptibility to deteriorations after infectious or stress stimuli." Han et al. (2021) concluded that maternal inflammation in pregnancy can program the fetal inflammatory pathways and epigenetic machinery, which could potentially result in increased expression of neurodevelopmental disorders in children. Factors of maternal immune activation triggered by inflammation can include factors such as obesity, gestational diabetes, pre-eclampsia, smoking, pollution, low socioeconomic status, depression, psychosocial stress, autoimmune disease, and asthma (Han et al., 2021). In a study by Rea et al. (2021), of the 62 PANS/PANDAS participants, 28 reported having relatives with psychiatric disorders, 7 reported having relatives with cardiovascular disorders, and 13 with metabolic disorders.

PANDAS Symptoms

Dean et al. (2015) states that post streptococcal movement and psychiatric disorders continues to expand from SC to now include tics, TS, OCD, and anorexia, among others. PANDAS is a clinical diagnosis, meaning there is no lab test to definitively diagnose PANDAS. Criterion for diagnosis of PANDAS includes the patient experiencing at least one of the three following: an acute and dramatic onset of obsessions and compulsions, experiencing an acute and dramatic onset of eating restrictions, and/or experiencing an acute and abrupt onset of motor and/or vocal tics (Kovacevic et al., 2015; McClelland et al., 2015; Snider & Swedo, 2004; Swedo et al., 2015). Comorbid symptoms must include at least two of the following: elevated anxiety or separation anxiety, emotion lability and/or depression, irritability, aggression, and/or severe oppositional behaviors, behavioral regression, sudden deterioration in school

performance (dysgraphia, decline in memory, math difficulty), motor movement changes, tics, or sensory abnormalities, and somatic signs including sleep disturbances or urinary frequency (McClelland, et al., 2015; Swedo et al., 2015; Kovacevic et al., 2015; Snider & Swedo, 2004).

Tourette Syndrome and Tics

One of the criteria for clinical diagnosis of PANDAS includes sudden onset of tic disorder. Tourette syndrome (TS) is a neurological disorder that causes sudden, repetitive, rapid, and unwanted movements or vocal sounds called tics. Tourette syndrome is one of a group of disorders of the developing nervous system called tic disorders. There is no cure for Tourette syndrome, but there are treatments to help manage symptoms. Tics caused by TS come and go across time, can be mild to severe, and are classified as simple or complex. Tics can be motor tics, which are tics that involve movement, or vocal tics, which involve sound. Simple tics are sudden, brief, repetitive movements that involve a limited number of muscle groups. Simple tics are more common than complex tics. Complex tics are distinct, coordinated patterns of movement that involve several muscle groups (Ueda & Black, 2021). Examples of simple motor tics can include eye blinking, facial grimacing, shoulder shrugging, and head or shoulder jerking (NIH, 2021). Examples of complex motor tics can include facial grimacing that includes a head twist and shoulder shrug. Complex motor tics can appear more purposeful, and can include things like hopping, jumping, or bending. Examples of simple vocal tics can include things like repetitive throat clearing, sniffing, barking, or grunting sounds. Examples of complex vocal tics may include things like repeating words

or phrases, or although more rarely, can include coprolalia, which is using vulgar, obscene, or swear words repetitively (NIH, 2021).

Many individuals with TS have additional co-occurring neuropsychiatric disorders, which can include ADHD, OCD, anxiety, learning disabilities, behavior or conduct issues, problems falling or staying asleep, social deficits, and sensory processing issues. TS is a clinical diagnosis in which doctors evaluate if there is presence of both motor and vocal tics that occur several times a day, every day, or intermittently for at least one year, onset of tics occurs before age 18, and the tics are not a side effect of medication or other medical conditions (Baglioni et al., 2019; Ueda & Black, 2021). Some people do not require treatment for TS if the tics do not interfere with their daily lives. Treatment options help to manage the symptoms but do not treat the underlying disease. Medications that block dopamine, alpha-adrenergic agonists, stimulant medications, and antidepressants are some of the commonly used medications to manage TS symptoms. However, these medications can all have serious side effects (Baglioni et al., 2019; Ueda & Black, 2021).

Chorea Movements

One of the comorbid symptoms in the diagnostic criteria of PANDAS includes motor tics and/or movements. Streptococcal infection has been shown to cause neuropsychiatric issues as well as choreiform movements. Chorea movements, whether in PANDAS or Sydenham Chorea, are arrhythmic, rapid, and often jerky movements (Murphy, et al., 2007; Singer, 2017). These movements can affect the entire body or only certain regions. Chorea movements can be challenging to diagnose as they can also

present in subtle ways or ways that just appear to be fidgety rather than chorea movements (Murphy et al., 2007; Singer, 2017).

Sydenham Chorea can show as a wide variety of symptoms following the streptococcal Group A infection. Sydenham Chorea involves both motoric and behavioral symptoms. Motoric symptoms are things like chorea and dysgraphia, which is decrease handwriting ability, and behavioral symptoms such as emotionality and anxiety (Murphy et al, 2007; Singer, 2017). PANDAS also presents as a wide variety of symptoms, such as anxiety, chorea movements including dysgraphia, decreased cognitive ability, and OCD (Murphy et al., 2007).

Murphy et al. (2007) sought to discover the rate of prevalence of chorea movement disorders after recent GAS infection and concluded that GAS infection did lead to higher rate of chorea movements. GAS has already been etiologically related to onset of Sydenham Chorea, Rheumatic Fever, and obsessive-compulsive disorder. In previous studies, streptococcal titers positively correlated with obsessive compulsive rate and severity. Murphy et al. (2007) also concluded that there was a positive relationship found between GAS infection and the incidence of Attention-Deficit Hyperactivity Disorder (ADHD).

Obsessive Compulsive Disorder

One of the three main criterion for PANDAS diagnosis includes sudden dramatic onset of obsessions and compulsions. Obsessive Compulsive Disorder (OCD) in children is characterized by recurrent and persistent thoughts, impulses, obsessions, and/or repetitive behaviors or compulsions that aim to prevent, reduce, or neutralize the anxiety

or distress caused by the obsessions (Rodriguez et al., 2019). The thoughts are the obsessions, and the behaviors are the compulsions. Symptoms of OCD can include:

- Unwanted thoughts, impulses, or reappearing images that occur repeatedly which lead to anxiety and distress
- Thinking about silently or repeating out loud certain words or phrases
- Repeating actions, such as frequent handwashing or placing things in certain order
- Having to complete certain tasks over and over according to rules in order to alleviate the obsession (Westwell-Roper & Stewart, 2019).

In children with OCD, children complete the behaviors associated with OCD because they think the behaviors will prevent bad things from happening or relieve anxiety in some way. However, the actual behavioral actions are typically not connected to any actual danger of bad things that happen. The behaviors can also be extreme, such as handwashing multiple times in one hour. Behaviors and compulsions can change over time. There is no cure for OCD, but there are treatment options available to help with symptoms. Treatment for OCD typically includes types of therapy, such as behavior therapy or cognitive-behavioral therapy (Westwell-Roper & Stewart, 2019).

Rodriguez et al. (2019) states that there is growing evidence that the immune system may play a role in the pathogenesis of OCD in patients with microglial dysfunction and autoimmune responses involving the levels of pro-inflammatory cytokines and anti-neuronal antibodies. In children with OCD, Rodriguez et al. (2019) found that there was a greater production of pro-inflammatory cytokines in children with OCD and that Positron Emission Tomography (PET) studies of these children indicated increased microglial activation in the neurocircuitry of OCD (Westwell-Roper & Stewart, 2019).

Attention-Deficit/Hyperactivity Disorder

Comorbid diagnostic criteria for PANDAS includes emotional lability and/or depression, irritability, aggression or severe oppositional behaviors, and sudden deterioration in school performance. This could be attributed to symptoms similar to those of Attention-Deficit/Hyperactivity Disorder (ADHD). ADHD occurs when a person shows a persistent pattern of inattention and/or hyperactivity-impulsivity that interferes with daily living and/or development (CDC, 2021). Practitioners use the American Psychiatric Association's Diagnostic and Statistical Manual, Fifth Edition (DSM-5) to help make an ADHD diagnosis. Using the DSM-5 helps create a standard of diagnosis and care for those suffering from ADHD. Symptoms of ADHD include inattention, hyperactivity, and impulsivity. In addition to displaying these symptoms, the following conditions must be met:

- Several inattentive or hyperactive-impulsive symptoms present before age 12
- Several symptoms present in multiple settings (home, school, work, etc.)
- Symptoms must interfere with or reduce the quality of daily life in social, school, or work functioning
- Symptoms are not easier explained by another condition, such as mood, anxiety, or personality disorders
- Symptoms can present as a combined presentation (NIH, 2021).

There is no cure for ADHD. Stimulants are the most widely used ADHD medications. Between 70-80% of children with ADHD have fewer ADHD symptoms when taking stimulants (CDC, 2021). Nonstimulants were approved for the treatment of ADHD; they do not work as quickly as stimulants, but their effect can last up to 24 hours (CDC, 2021).

Behavior therapy is another treatment option for ADHD and is used to modify behaviors in varying situations to reduce symptom exacerbation (CDC, 2021).

Autism Spectrum Disorder

Comorbid diagnostic criteria for PANDAS include emotional lability and/or depression, irritability, aggression or severe oppositional behaviors, sudden deterioration in school performance, and sensory abnormalities. This could be attributed to symptoms similar to those of autism spectrum disorder (ASD). ASD is a group of neurodevelopment dysfunctions causing behavioral abnormalities in social, verbal, and non-verbal communication (Huxley et al., 2017). The etiology of ASD is unknown but is hypothesized to be the outcome of a combination of genetic, neurological, environmental, and immunological factors (Huxley et al., 2017). In a study by Huxley et al., (2017), researchers aimed to established functional interactions between the targets of auto-antigens produced as a result of GAS, and genes linked to ASD, via genome wide association studies. Huxley et al., (2017) discovered that there is a relationship between immune and autoimmune responses caused by GAS infection associated with ASD. Symptoms of Autism Spectrum Disorder (ASD) can include, but are not limited to,

- Avoiding eye contact
- Having little interest in other children or caretakers
- Limited display of language
- Being upset by minor changes in routine

Autism Spectrum Disorder can sometimes be detected as early as 18 months of age, but more typically happens around the second year. Diagnosis by an expert at age two is considered very reliable (CDC, 2021). Children with ASD can have difficulty making

and maintaining friendships, difficulty understanding social expected norms, and can have co-occurring conditions such as ADHD, OCD, anxiety, and/or depression. There is no cure for ASD. The Food and Drug Administration has approved the use of risperidone for treatment of ASD symptoms in children, and this treatment works best when combined with therapy to maximize the child's functioning and reducing the symptoms of ASD (NIH, 2021). Huxley et al. (2017) states that further experimental research into potential autoimmune etiologies of ASD is needed. Goncalves et al. (2018) states that manifestations of ASD are considered to have neuroimmune etiology, and describes a case study of a six-year-old male patient who was incorrectly diagnosed ASD but in fact had PANDAS. The patient was treated with IVIG and reached complete remission of symptoms (Goncalves et al., 2018).

Anxiety

Anxiety and separation anxiety are comorbid symptoms in the diagnostic criteria of PANDAS. Anxiety is persistent or extreme fears that can happen in both adults and children. When children do not outgrow the fears or when the fears persist and interfere with daily life, children may have an anxiety disorder. Anxiety in children can include:

- Separation anxiety
- Phobias
- Social Anxiety
- Generalized Anxiety
- Panic Disorders

Anxiety typically presents as fear and worry, but can also include rage, anger, and irritability. Anxiety can be challenging to diagnose in children as it may be the result of

other disorders or trauma. It is important for practitioners to investigate all possible causes when diagnosing anxiety in children (CDC, 2021). Any child can develop anxiety, but it is highly more likely in children who have biological disorders, experience stress or trauma, maltreatment, or if the anxiety is hereditary from parents (CDC, 2021). Behavior therapy and cognitive behavioral therapy are two of the widely used treatment plans for children suffering with anxiety, in addition to eating a healthy diet, getting plenty of sleep, and physical activity.

Dysgraphia and Academic Decline

A comorbid diagnostic symptom of PANDAS is academic decline. Dysgraphia is a learning disorder in which the child's writing skills are not where they are expected to be given their age and cognitive level (Chung & Patel, 2015). Academic decline in PANDAS patients can present as dramatic handwriting changes, decline in memory, and/or decline in math skill. Dysgraphia can present on its own but can typically occur with other neuropsychiatric issues (Chung & Patel, 2015). Dysgraphia can often go misdiagnosed or incorrectly managed due to the lack of understanding of potential cause. Chung and Patel (2015) state the importance of proper diagnosis and intervention from family care providers.

Eating Restrictions

One of the three main criterion for PANDAS diagnosis includes acute and dramatic onset of eating restrictions. This can include significant weight loss, fear of food contamination, obsessions about healthy eating, and fear of eating (Calkin & Carandang, 2007). Anorexia is a severe psychiatric disorder. Tasaka et al. (2017) states that childhood and adolescent onset of anorexia should be much more closely followed up on

because of comorbid symptoms as well as long-term follow up needs. Anorexia nervosa includes both the restricting subtype of eating disorder and the binge/purge subtype of eating restriction. The most prevalent in childhood onset anorexia is the restricting subtype (Tasaka et al., 2017).

PANDAS Diagnosis

Understanding the various other neuropsychiatric syndromes is important in the understanding of PANDAS. In cases of PANDAS, the above listed neuropsychiatric disorders are symptoms that develop as a result of basal ganglia inflammation and are not stand-alone diseases. PANDAS. The aforementioned diseases have standards of care implemented and are accepted by the medical community, while PANDAS is frequently misdiagnosed. PANDAS requires a clinical diagnosis, meaning there is no laboratory test that can diagnose PANDAS.

Clinical Diagnosis

Clinical diagnosis of PANDAS is defined by: presence of significant obsessions, compulsions, and/or tics, abrupt onset of symptoms or a relapsing-remitting course of symptom severity, pre-pubertal onset, association with streptococcal infection, and association with other neuropsychiatric symptoms (Snider & Swedo, 2004). PANDAS can present with a wide variety of neuropsychiatric symptoms, including abrupt onset of OCD, extreme food restriction, tics, and accompanying symptoms, which can include:

- Anxiety
- Emotional lability and/or depression
- Irritability, aggression, and/or oppositional behavior
- Behavioral regression

- Deterioration in academic performance
- Sensory sensitivities
- Motor movement abnormalities
- Somatic symptoms, such as sleep disturbance or urinary frequency

(Pandas Network, 2021).

PANDAS is a clinical diagnosis in which doctors use the PANDAS Physicians Network diagnostic flowchart to make a diagnosis (PPN, 2020). Cases of PANDAS can be mild, moderate, to severe. In a mild case of PANDAS, symptoms are significant and cause disruptions at home and/or school and occupy a few hours per day (PPN, 2020). In moderate cases of PANDAS, symptoms are distressing to the child, interfere with daily activities, and occupy 50-70% of time each day during waking hours (PPN, 2020). In severe PANDAS cases, symptoms are incapacitating, life threatening, and/or occupy 71-100% of time during waking hours (PPN, 2020).

Cunningham Panel

The Cunningham Panel was developed by Dr. Madeleine Cunningham and is overseen by Moleculera Labs. According to the Moleculera Labs website, the Cunningham Panel is a series of blood tests that can assist clinicians in diagnosing infection-triggered autoimmune neuropsychiatric syndromes, such as Basal Ganglia Encephalitis and PANS/PANDAS. PANDAS is a clinical diagnosis, but Cunningham Panel test results can be supportive of a clinical diagnosis by providing evidence of an underlying autoimmune issue which can also help guide treatment methods (Moleculera Labs, 2021). The Cunningham Panel consists of five blood tests, including:

- Anti-Dopamine D1 Receptor

- Anti-Dopamine D2L Receptor
- Anti-Lysoganglioside-GM1
- Anti-Tubulin
- Calcium/calmodulin-dependent protein kinase II (CaMKII)

According to the Moleculera Labs website, four of the five blood tests measure the levels of circulating autoantibodies in serum that are directed against and bind to, or block, specific neuronal targets in the brain. Each of these autoantibodies have been associated with the presence of various neurologic and/or psychiatric symptoms. When autoantibodies bind to or block these targets, they can disrupt normal neuronal functioning, resulting in the onset of neuropsychiatric symptoms. Elevated levels on one or more of these tests indicate that a person's neuropsychiatric symptoms may be due to a treatable autoimmune disorder, rather than a classic neurologic or psychiatric illness. The Cunningham Panel is considered a metabolic test; therefore, the laboratory results represent the values at the time the patient's blood was collected, which may vary over time, with treatment, and in conjunction with the presence or absence of symptoms.

There is much controversy surrounding the effectiveness of the Cunningham Panel (Hesselmark & Bejerot, 2019; Hesselmark & Bejerot, 2017; Shimasaki et al., 2020). In a study by Shimasaki et al. (2020), the results of the Cunningham Panel were able to correlate with neuropsychiatric symptom changes, while a study by Hesselmark and Bejerot (2017) concluded that the use of the Cunningham Panel for PANDAS diagnosis is not supported by evidence in their study. As the usefulness of the Cunningham Panel remains inconclusive and controversial, PANDAS remains a disorder that requires clinical diagnosis.

Barriers to Diagnosis

LaRusso et al., (2022) discusses gaps in diagnosis and care due to logistics of medical coverage thus compromising children's health and development. LaRusso et al., (2022) states that patients with PANS/PANDAS often receive untimely care that is not covered by insurance. LaRusso et al., (2022) concludes that the for-profit structure of the healthcare system in the United States results in costly and lengthy paths to treatment and diagnosis for PANS/PANDAS patients. LaRusso et al. (2022) states that insurance coverage in the United States for PANS/PANDAS depends on legislation, advocacy, clinical characteristics of each child, and how for-profit insurance companies react to an increased demand for services. In addition, many practitioners do not acknowledge the condition or offer effective treatments. LaRusso et al. (2022) concludes that the financial motivations of insurance companies across modern health care systems imposes restrictions that impede access to care for those suffering with PANS/PANDAS. Therefore, untimely care, the time gap from PANS/PANDAS symptoms to diagnosis and treatment is the result of the modern logistics that structure the medical and insurance fields. The results of the study by LaRusso et al. (2022) demonstrate how modern medicine and various facets of insurance coverage fail to protect families of children with PANS/PANDAS against catastrophic expenses, and block care that would prevent developmental disruptions and losses, associated suffering of child and family, and save cost to the health care system.

PANDAS Treatment

Therapy and prescription drugs are typically recommended for the disorders that present with PANDAS, such as OCD or anxiety. However, these treatments fail for

children suffering from PANDAS as these treatments treat only the symptoms, not the underlying cause, of the condition. Typically, cognitive behavior therapy and selective serotonin reuptake inhibitors are the therapies to treat OCD (Sigra et al., 2018). However, for a large portion of PANDAS sufferers these treatment methods are not enough since they do not treat the underlying autoimmune disorder. In the study by Prasad et al. (2021), researchers investigated which treatments would be most effective and satisfactory for treating PANDAS, which includes treating the underlying autoimmune disorder. Treatment for PANDAS focuses on eliminating the autoantibodies from circulation (Platt et al., 2017). Swedo et al. (2017) states that in particularly severe cases of PANDAS that do not respond to drug and behavioral therapy, immunomodulating therapies individually or in combination with corticosteroids, rituximab, intravenous immunoglobulin, plasmapheresis, and mycophenolate can be used. However, this should be with caution, as Williams et al. (2016) notes that steroids used to improve OCD symptoms can worsen tics.

Although further information is needed to distinguish brain changes brought on by inflammation causes by the immune system, Cooperstock et al. (2017) compiled information to help create more systematic, practitioner evidence-based criteria to both diagnose and treat PANS/PANDAS. Cooperstock et al. (2017) uses information from treating rheumatic fever, Sydenham chorea, and practitioner experience with PANS/PANDAS. Leonard and Swedo (2001) use practitioner expertise and a literature review to provide a proposed model of pathophysiology of PANDAS in order to guide diagnosis and treatment. In studies by Prasad et al. (2021) and Calaprice et al. (2018), subjects were most commonly treated with antibiotics (n=60, n=675). In the study by

Prasad et al., (2021), tonsillectomy was the second most occurring treatment (n=50), then intravenous immunoglobulin (IVIG) (n=24), then prescription Rituximab (n=9), steroids (n=12) and plasma exchange (n=6). The study did not discuss what type of antibiotics were used so no correlations on antibiotic brand efficacy could be established from this study. In the study by Calaprice et al. (2018), different brands and doses of antibiotics and IVIG were examined. In the study by Calaprice et al. (2018), no form of psychotherapy was considered to be very effective.

In the study by Prasad et al. (2010), there was no significant difference found in frequency of the 10 surveyed symptoms except for choreiform movement. There was a significant time effect on the symptoms classified as obsessive compulsions, tics, frequent urination, trouble sleeping, general anxiety, dysgraphia, aggressive behavior, behavior regression, and intrusive thoughts. Regardless of treatment type, all parents reported a decrease in symptoms within the course of the year after treatment. With the exception of choreiform movements, there was a reduction in frequency of all symptoms over the year after diagnosis, regardless of treatment type.

Symptom exacerbations, commonly known as flares, are common in PANS/PANDAS patients and can be caused by upper respiratory infections, influenza, mycoplasma pneumoniae, lyme, gastrointestinal infections, dental infections, enterovirus, and allergies (Cooperstock et al., 2017). In a study by Latimer et al. (2015), symptom exacerbations treated with corticosteroids tended to last 4 weeks less than symptom flares not treated with corticosteroids.

Antibiotics

In rheumatic fever and Sydenham chorea, treatment involves long-term antibiotics

to treat the infection as well as prophylactically prevent future infection. Treatment of PANDAS typically begins with antibiotics, and involves long-term antibiotics used to prevent recurrent infection. Cooperstock et al. (2017) provides a dosing chart with recommendations on brands of antibiotics and what to use if there is allergic reaction. This is an important part, as some antibiotics are found more useful in fighting streptococcal infections and the ability to treat neuropsychiatric disorders as a result of bacteria than others (Cooperstock et al., 2017). Cooperstock et al. (2017) notes that use of antibiotics prophylactically in PANDAS patients does not have complete evidence, but notes that the potential benefit could be the possibility of preventing neural injury from future GAS infections. In a case study by Ayadin and Abali (2010), early antibiotic treatment was useful in treatment of PANDAS. In a study by Demesh et al. (2015), antibiotics alone improved children suffering with PANDAS from a baseline of 10, worst severity, to a score of 8. In a study by Rea et al., (2021) nearly all children in the retrospective study were treated with antibiotics (56 of 62 participants). However, this same study concluded that antibiotics did not have a significant effect on improving tics or OCD symptoms. In a study by Rea et al., (2021), antibiotics helped temporarily reduce OCD and tics, but did not have long lasting effect. In a study by Calaprice et al. (2018), the majority of participants (n=675) were treated with antibiotics, and it was concluded that a treatment course of >30 days produced the best results with 52% of participants reporting it was a very effective treatment.

Plasmapheresis and Intravenous Immunoglobulin

In a study by Perlmutter et al. (1999) children with severe, misguided immune response to infection were treated with either plasma exchange, intravenous

immunoglobulin (IVIG), or placebo. Perlmutter et al. (1999) studied if plasma exchange or IVIG would be more effective than placebo at reducing the neuropsychiatric symptoms. Twenty-nine children completed the trial. Ten children received plasma exchange, nine children received IVIG, and 10 children received placebo. At one month post treatment, the IVIG and plasma exchange groups showed significant improvement in neuropsychiatric symptoms (Perlmutter et al., 1999). In a study by Calaprice et al. (2018), plasmapheresis was reported as having a positive initial response (n=25), but did not create long-lasting effect.

In a study by Kovacevic et al. (2015), IVIG was used as a therapeutic approach for twelve children in a case study. All 12 children benefited from IVIG administration, even when symptoms had been present for several years prior to treatment (Kovacevic et al., 2015). In a retrospective study of therapeutic plasma exchange therapy by Latimer et al. (2015), 78% of respondents had significant reduction in symptom severity. Many immunotherapies such as plasmapheresis and IVIG can take weeks to months to show effectiveness (Platt et al., 2017). In a study by Rea et al. (2021), intravenous immunoglobulin was not an effective treatment for the OCD in PANDAS patients. In a study by Calaprice et al. (2018), 193 participants had received IVIG treatment and reported that it was at least somewhat effective as treatment, but for 18% of these participants the effects were not sustained. Sigra et al. (2018) states that IVIG as a treatment method remains inconclusive due to double-blind studies showing low support of this treatment. In a study by Pavone et al. (2020), on the effectiveness of IVIG for PANDAS, all patients were classified with extreme grade of PANDAS, a noticeable improvement of symptoms was evident for at least one year in 47 out of the 55 patients,

11 of these showed an evident symptoms remission in a single attempt, and the remaining required a second administration to notice lasting symptom improvement.

Tonsillectomy and Adenoidectomy

Sigra et al. (2018) notes various studies using tonsillectomy and adenoidectomy for treatment of PANDAS, but notes that observational studies only provide weak evidence for tonsillectomy and/or adenoidectomy being weak for PANDAS treatment. A study by Harabuchi and Takahara (2019) notes the tonsil-induced autoimmune and inflammatory response regarding the tonsillar Th17 cells. Harabuchi and Takahara (2019) were able to link the overactive Th17 tonsil cells to the autoimmune and inflammatory markers due to a hyperimmune response. To date, there has not been a controlled case study using tonsil/adenoidectomy as a treatment for PANDAS. Prasad et al. (2021) points out these that even without antibiotic treatment, tonsillectomy and adenoidectomy alone can show symptom improvement. In a case report by Alexander et al. (2011), tonsillectomy was performed on a child with PANDAS and at one year follow up, the patient had not suffered from recurrent streptococcal infection and the neuropsychiatric symptoms had resolved completely. In another case study by Caletrio et al. (2008), a case report of a nine-year-old who had received tonsillectomy had no further symptoms after surgery. In a study by Demesh et al. (2015), children who underwent tonsillectomy had improved at all measured periods post-surgery. Demesh et al. (2015) found that after tonsillectomy, four out of nine children had complete recovery with tonsillectomy, and five out of the nine reported a baseline score of three for their symptoms, with all of them measuring 10, worst severity, prior to surgery.

Corticosteroids

Sigra et al. (2018) notes that corticosteroids can be an effective treatment and can reduce the length of symptom exacerbations. In a study by Brown et al. (2017), flares treated with corticosteroids typically lasted 4 weeks less than the 12.2 weeks without corticosteroid use (Sigra et al., 2018). Brown et al. (2017) concludes that non-steroidal anti-inflammatory drugs given prophylactically at flare onset may shorten the neuropsychiatric symptom duration during a flare. Several case reports exist on PANS/PANDAS treatment using corticosteroids, with some noting they are very effective and others not effective due to increase in negative side effects (Sigra et al., 2018). Since PANDAS serves as a forme fruste of SC, similar treatments may be effective. A study by Fusco and Spagnoli (2018) found that corticosteroids were effective in both short and long-term treatment of SC. A study by Favaretto et al. (2020) concluded that corticosteroid treatment was effective for SC. Corticosteroids are typically used in combination with other therapies, such as IVIG or antibiotics. Lack of double-blinded placebo-controlled studies makes corticosteroid use in PANDAS treatment inconclusive (Brown et al., 2017; Spartz et al., 2017). A study by Calaprice et al. (2018) concludes that steroid therapy, including over the counter anti-inflammatories, was at least somewhat effective for the majority of participants.

Psychotropic Drugs and Psychotherapy

Members of the PANS/PANDAS research consortium shared their clinical experiences to develop treatment guidance for psychotropic drugs and psychotherapy interventions in PANS/PANDAS (Thienemann et al., 2017). In a study by Rea et al. (2021), 33 of 62 participants had received cognitive behavioral therapy (CBT) techniques

that did show a significant improvement on OCD symptom severity, but did not have significant improvement on tics. Rea et al. (2021) concluded that symptomatic therapy such as haloperidol, risperidone, aripiprazole, clozapine, methylphenidate chloridrate, and pimozide were administered in 15 of 62 participants but the therapies did not have significant effect on tics or neuropsychiatric symptoms. In a study by Calaprice et al. (2018), psychotropic medications, most commonly SSRIs, were reported as having been used but reported as ineffective. The study by Calaprice et al. (2018) also concluded that CBT was reported to at least be somewhat effective to those treated with this method. Thienemann et al. (2017) states that the timing of CBT is important, as during particular symptom flares the child may be unable to fully participate due to PANDAS symptoms, but the sooner the intervention begins the more likely it will be helpful. Unlike other conclusions, Wilbur et al. (2019) gives the recommendation that children presenting with PANS/PANDAS should be treated with psychotropic medication and will be expected to show improvement similar to that of children receiving psychotropic medication without PANS/PANDAS. Thienemann et al. (2017) concluded that until further research has been conducted on PANS/PANDAS specific psychiatric interventions, practitioners must rely on treating PANS/PANDAS patients with standards of care used for the various symptoms in non-PANS/PANDAS patients.

Remission

Felson (2011) describes remission as a state of being, and as the absence of disease activity. In other diseases, such as rheumatoid arthritis, absence of disease activity is what some would consider an unattainable goal. Felson (2011) states that remission is more generally operationalized as either complete absence of disease activity

or a level of disease activity that is so low it is no longer troublesome to the patient. Future research is needed to better understand the aim of remission in PANDAS, how to attain remission, and a clear definition of remission in PANDAS such as complete remission or complete remission on treatment, and what treatments, if needed, can be used for remission maintenance.

Remission in other Autoimmune Diseases

Systemic Lupus Erythematosus (SLE) and Rheumatoid Arthritis (RA) are both autoimmune inflammatory diseases. Remission is typically the ultimate goal in any disease, but various studies take different approaches to the definition of remission. In a study on remission experiences in SLE, Wilhelm et al. (2021) describes four different definitions of remission, including clinical remission, complete remission, clinical remission on treatment, and complete remission on treatment. Like PANDAS, SLE often follows a relapsing-remitting pattern. The study by Wilhelm et al. (2021) found that achieving remission was frequent, but durable remission was rare. In SLE, the median duration of remission for all definitions of remission was only 3 months (Wilhelm et al., 2021). According to Doria et al. (2016), it is possible that remission may not be a suitable target for some diseases, as in the case of SLE.

Another issue with the concept of remission is how to manage patients once remission is achieved. According to Gul et al. (2021), medical advancements have led to more promising outcomes of disease remission in RA; however, there is little guidance on how to manage patients once remission is achieved. In a study by Wilhelm et al. (2016) examining remission of SLE, the median time to remission varied based on the definition of remission. Using the definition of clinical remission, the median time to

reach remission was 8.7 years (Wilhelm et al., 2021). Using the definition of complete remission, the median time to reach remission was 11.0 years (Wilhelm et al., 2021). Using the definition of clinical remission on treatment, the median time to reach remission was 1.8 years (Wilhelm et al., 2021). Using the definition of complete remission on treatment, the median time was 3.1 years (Wilhelm et al., 2021). The median time the remission was sustained was similar with all four definitions at 105 days (Wilhelm et al., 2021). This study not only sheds light on the need for clear definitions of remission, but also the importance of further studies related to remission management and treatment options.

Remission Experiences for Children and Families

Studies of other childhood illness offer guidance related to family and child experiences in dealing with disease and remission. Reinfjell et al. (2009) conducted a study on children in remission from leukemia regarding their mental health, psychosocial adjustment, and parental functioning. Reinfjell et al. (2009) concluded that all children in the study (N=40) were children in remission from leukemia and all showed significantly more problematic issues regarding mental health and psychosocial adjustment, according to their parents' perception, compared to healthy controls. The length of treatment for childhood leukemia can vary but is an average of 2.5 years. This time period can create an enormous amount of stress during treatments and can isolate children away from their peers for long periods of time. A study by Drotar (1997) states that parental functioning is one of the strongest contributors to adjustment in children with chronic health conditions. According to Reinfjell et al. (2009) and Maurice-Stam et al. (2008), emotional distress among parents remains heightened compared to healthy controls for one year after end of

treatment, but then begins to decrease over time. Reinfjell et al. (2009) states that a significant number of parents will still suffer from clinical distress five years post-treatment. Another element of reaching remission during childhood is the discussions parents must have with their child about the possibility of the disease returning. Murphy et al. (2020) studied how mothers and children discuss possible cancer recurrence in childhood cancer survivors. Murphy et al. (2020) examined discussions mothers have with their children related to fears of cancer recurrence. Examining these discussions can help guide predictors and communication cues for families to support them through fear of recurrence conversations. These studies shed light on the importance of adequate rehabilitation for children in remission.

In a study by Erbis et al. (2018) the daily life struggles for children, adolescents, and adults living with autoimmune diseases was investigated. Erbis et al. (2018) concluded that unmet needs of those living with autoimmune diseases impacts all areas of life, with the most relevant unmet needs happening within the school and health care systems. Rea et al. (2021) noted that worsening school performance, increased anxiety, irritability, and aggressivity all increase with symptom exacerbations. In a study by Vlist et al. (2019) researchers sought to understand participation in childhood in those with chronic disease. Vlist et al. (2019) found that children with chronic disease learn to carefully weigh participation against their current and/or future needs and assess the risk versus benefit of their choices and chronic condition needs. Vlist et al. (2019) states that children view participation as more than just engaging in an activity, but having a sense of belonging and the ability to influence social interactions and keep up with their peers.

Tona et al. (2017) conducted a study to determine what problems arise in terms of occupation, body functions, and performance skills during PANS or PANDAS symptom exacerbations. This study concluded that children present with pervasive occupational performance needs during exacerbation periods and that children may benefit from accommodations to maximize function during these periods (Tona et al., 2017). Frankovich et al. (2019) studied PANS symptom severity and its relation to caregiver burden. Frankovich et al. (2019) concluded that PANS caregivers suffer high caregiver burden, and the severity of the PANS syndrome predicts increased caregiver burden. Erbis et al. (2018) recommends that it is an urgent need to increase societal knowledge and empower patients as well as create supportive environments at school and work to help ensure successful participation of those with autoimmune diseases have their psychosocial needs met. Maurice-Stam et al. (2008) states that the time when a child's treatment ends and remission begins is typically a difficult and anxious time for both the minor patient and their parents, as during this time the social and emotional support from other's decreases but the family is just beginning their journey in coming to terms of what has happened. Murphy et al. (2020) states that 62% of adolescent and young adult cancer survivors reported clinically significant levels of fears that their cancer will return. Murphy et al. (2020) states that the fear of cancer recurrence is associated with a range of difficulties that can include impaired psychological functioning, poor health-related quality of life, greater healthcare utilization, and maladaptive health behaviors.

Ringer and Roll-Pettersson (2022) discuss some feelings of parent experiences when dealing with a child with PANS/PANDAS. Themes that emerged from the study by Ringer and Roll-Pettersson (20220) included categories such as:

- he/she was a completely different child
- their suffering is unbearable
- unable to parent their other children
- continuous and clear care plans are hard to get
- parents are blamed
- trying to make up for lost childhood

Ringer and Roll-Pettersson (2022) state that parents of children with relapsing and remitting symptoms often tried to compensate for lost time and create enjoyable moments with the child when he/she was not in a symptom flare as a way to give back the lost childhood and attempt to compensate for their suffering. However, Ringer and Roll-Pettersson (2022) distinguish children that have a static symptom course, rather than remitting, are unable to have these moments as parents indicate they are not able to live normally for even small amounts of time due to always dealing with the illness.

PANDAS Remission

PANDAS is considered to have a relapsing and remitting pattern, where exposure to bacteria or virus can induce symptoms, and symptoms wax and wane over time, known as symptom flares or symptom exacerbations. Cooperstock et al. (2017) states that symptom exacerbations are common in PANS/PANDAS patients and can be caused by upper respiratory infections, influenza, mycoplasma pneumoniae, lyme, gastrointestinal infections, dental infections, enterovirus, and allergies. There is little literature related to symptom flares, their duration, and what to do to manage them. In a study by Leon et al. (2018), at follow-up, 29 of the 33 participants were experiencing no or only subclinical OCD symptoms. Of the remaining 4 with clinically significant OCD symptoms, one

child was currently experiencing a symptom exacerbation at the time of follow-up, one child had discontinued all treatments before all symptoms had resolved, and two children had persistent OCD and remained in treatment (Leon et al., 2018). In a study by Colvin et al. (2021), the cognitive, graphomotor, and psychosocial challenges PANDAS patients faced were ongoing and significant academic difficulty and emotional, behavioral, and social concerns remained after symptom resolution. In a retrospective study of 40 patients, Latimer et al. (2015) concluded that improvement with therapeutic plasma exchange was not associated with the duration of illness. This finding needs further research, as this could imply that the damage inflicted from PANDAS is able to be treated regardless of how long the symptoms were present. In a study by Gruijter et al. (2021), a bidirectional relationship between puberty and autoimmune rheumatic disease was found. In a case study by Cross et al. (2021), the researchers conclude that after a span of 31 months of illness and treatment with antimicrobials and IVIG, the patient reached complete remission.

When children experience PANDAS flares, they often require individualized education plans at school in order to accommodate their PANDAS symptoms. In a study by Latimer et al. (2015), symptom exacerbations treated with corticosteroids tended to last 4 weeks less than symptom flares not treated with corticosteroids, which tended to last 12 weeks. In a study by Shimasaki et al. (2020), the results of the Cunningham Panel were able to correlate with neuropsychiatric symptom changes during symptom exacerbations. A study by Lepri et al. (2019) concluded that infection-related relapses were observed in 167 out of 371 participants long-term. The Pandas Physicians Network recommends, even in severe cases, that after treatment has been successful, a specialist is

needed in order to manage flares. Mohammad and Dale (2018) find in PANS/PANDAS patients, there is a risk of relapse in the majority of patients. It is not clear if symptom exacerbation management is life-long or if remission includes complete symptom recovery with no further exacerbations. Defining remission in PANDAS could be helpful in the future.

Ringer and Roll-Pettersson (2022) describe the effect of PANS/PANDAS on families by exploring parental stress. Ringer and Roll-Pettersson (2022) identified five categories of parents' experiences related to the stress of dealing with a child with PANS/PANDAS, including, "being effected by the symptoms, experiencing the symptoms over and over again, having no control, obtaining medical treatment being challenging, and managing problems." The study by Ringer and Roll-Pettersson (2022) highlights the effect of PANDAS on the family system and is a gateway to future research on how to minimize family issues related to the disorder.

Long-Term Outcomes

Few studies shed light on the long-term outcomes of children with PANDAS. Although there is a consensus on standard of treatment, long-term outcomes of these treatment methods are unknown. In a study by Leon et al. (2018), 33 children with PANDAS participated in follow-up interviews after treatment. After an average of 3.3 years after baseline evaluation, 88% of participants were in complete or nearly complete remission (Leon et al., 2018). However, most children, 72%, had at least one symptom exacerbation of PANDAS during the three-year follow up period. These exacerbations were typically less severe and generally short-lived compared to the baseline episode (Leon et al., 2018). During symptom exacerbations, a variety of treatments were used,

including all or combinations of antibiotics, immunomodulatory therapies, and cognitive behavioral therapies (Leon et al., 2018). At the follow-up, 29 of the 33 participants were experiencing no or only subclinical OCD symptoms. Of the remaining 4 with clinically significant OCD symptoms, one child was currently experiencing a symptom exacerbation at the time of follow-up, one child had discontinued all treatments before all symptoms had resolved, and two children had persistent OCD and remained in treatment (Leon et al., 2018). In a study by Colvin et al. (2021), the cognitive, graphomotor, and psychosocial challenges PANDAS patients face were ongoing and significant academic difficulty and emotional, behavioral, and social concerns remained after symptom resolution.

A study by Lepri et al. (2019) concluded that infection-related relapses were observed in 167 out of 371 participants long-term. Mohammad and Dale (2018) concluded that the majority of PANS/PANDAS patients will have relapse, persistent OCD, and tics. Mohammad and Dale (2018) also conclude that in PANS/PANDAS patients the speed of recovery is typically rapid, whereas in other immune-mediated movement disorders, such as SC, can take months to years.

Gromark et al. (2022) concluded that complete remission was rare (n=34), however, the majority of children did improve over a 3-year follow-up period. Gromark et al. (2022) also found that a minority of patients that displayed a chronic-static/progressive course that required additional treatments. The operationalized definitions of flare and clinical course were able to distinguish the chronic and non-chronic groups of participants. This information will be useful as a basis in future studies related to treatment and prognostic guidelines.

The aforementioned studies create a starting point for this study. Very little is known about the remission of PANDAS. Based on these studies, it seems the factors in PANDAS remission, as well as what typical remission and subsequent symptom exacerbations looks like, can vary or remains unexplained. There are also many factors of remission in PANDAS that have yet to be explained, such as lasting psychosocial issues of the child and parents and remission management plans. This study will take a qualitative approach to parents' perceptions of factors of remission in PANDAS, that could lead to future research detailing what treatments lead to remission and how to best treat symptom exacerbations, should they continue into remission.

Biblical Foundations of the Study

As the aim of this study was to gain parents' perceptions of PANDAS remission, this study provides hope for parents currently battling PANDAS and provides them with information to help them persevere. A study by Maurice-Stam et al. (2008) on emotional functioning of families during remission of pediatric cancer found that parents who were optimistic about the further course of their child's disease reported fewer emotional problems, evidence of the importance of keeping hope and faith in mind when dealing with the illness of a child. In 1 Thessalonians 1:3, Paul is addressing the church and expressing his gratitude in their response to the gospel. He mentions their work of faith, labor of love, and steadfast hope. God's grace had saved them when they put their faith in Christ instead of endeavoring to be saved by their own efforts, and the same grace had produced in them the good works God had intended to produce in their lives. 1 Thessalonians 1:3 says, "We remember before our God and Father your work produced by faith, your labor prompted by love, and your endurance inspired by hope in our Lord

Jesus Christ." This scripture could be a direct example of the faith, hope, and love PANDAS parents rely on in pursuit of care and healing for their children. As parents faithfully hope for remission for their children, Romans 5:5 says, "And hope does not put us to shame, because God's love has been poured out into our hearts through the Holy Spirit, who has been given to us." As doctors and insurance agencies and other facets of the medical system can cause disruption and delay for medical healing, this is man's word, not the Word of God. In Psalm 3:2-6 the Bible says, "Many are saying of me, 'God will not deliver him,' But you, Lord, are a shield around me, my glory, the One who lifts my head high. I call out to the Lord and he answers me from his holy mountain. I lie down and sleep, I wake again, because the Lord sustains me. I will not fear though tens of thousands assail me on every side." Both parents and the children suffering with PANDAS must remain steadfast in their hope, faith, and love.

Biblical Worldviews of the Study

Using Johnson's (2010) *Five Views,* and Wolter's (2005) *Creation Regained,* the transformational worldview approach of this study operates under the premise that God gave scientists the minds that are able to comprehend and do great scientific work, and that it is their duty to carry out ethical science morally. Johnson (2010, p. 225) concludes by saying that the Transformational View is not about trying to make two separate disciplines, as in faith and science, relate. Rather, the Transformational View is the study of psychology through faith and contemplating God in the process. The researcher approached this study with the goal of discovery and helping others as told to do in 2 Timothy 3:17, "That the man of God may be competent, equipped for every good work." The researcher approached the study of PANDAS as a way to provide testimony for

drawing closer to God. In doing so, the researcher aims to be a servant to child development, families, youth mental health, and families struggling with pediatric illness such as PANDAS. The researcher aims to provide sound research and define areas for future research for PANDAS families, as 1 Samuel 15:13, “The Lord bless you, I have carried out the Lord’s instructions.”

Biblical References of the Study

The story of Elisha and Naaman in 2 Kings discusses how illness does not discriminate between people. Naaman, the commander of the Syrian army, fell ill with leprosy. Naaman’s pride nearly kept him from receiving healing. This is similar to parents of PANDAS patients, as many will try to do all within their power to help their children. Parents of sick children plead to God for answers and healing, and must learn to be patient and accept the path God has laid out for them. This does not mean parents cannot read and equip themselves with the science that is available related to PANDAS, as God created the scientists that study PANDAS. Proverbs 24:14 states, “Know also that wisdom is like honey for you: If you find it, there is a future hope for you, and your hope will not be cut off.” This study on remission will provide education and hope for parents of children with PANDAS. With the wisdom from scientific literature and the foundations of the Bible, parents on the path to remission for their children will have the understanding that like all things in life, PANDAS exacerbations are a season. Ecclesiastes 3:1-8 explains how everything in life has a season. In the season of PANDAS, and hoping for remission, the Bible says in Isaiah 40:31, “But those who hope in the Lord will renew their strength. They will soar on wings like eagles; they will run and not grow weary; they will walk and not be faint.”

In Jeremiah, Israel was exiled for disobedience. A false prophet had told the people of Israel that God would deliver them within two years' time. Jeremiah delivers the news that Israel will be in exile for seventy years. This is not what the people of Israel wanted to hear. God wants the people to know that he still has a plan for them, even when they are facing a dark situation. The people must hold on to hope that God is not finished with them. Romans 12:12 says, "Be joyful in hope, patient in affliction, and faithful in prayer." As time drags on, such as the seventy years in Israel or waiting on PANDAS healing, parents can be reminded of hope in the face of trouble, as the Bible tells in Romans 8:24-25, "Who hopes for what they already have? But if we hope for what we do not yet have, we wait for it patiently." This tells PANDAS parents to wait patiently for remission and healing for their children. Isaiah 43:18-19 says, "Forget the former things; do not dwell on the past. See, I am doing a new thing! Now it springs up; do you not perceive it? I am making a way in the wilderness and streams in the wasteland." Hope requires the belief from PANDAS parents that God provides and cares for their children, and will keep moving toward remission. The Bible has many stories related to people persevering through hard times with hope and faith in God. The Scripture can encourage PANDAS parents to keep asking, seeking, and knocking using scientific foundations and the hope that God's deliverance from PANDAS is imminent. As PANDAS families endure the wax and wane symptom exacerbations and various treatments, the Bible tells the story of Paul and persevering through troubles for eternal glory. 2 Corinthians 4:16-18 states, "Therefore we do not lose heart. Though outwardly we are wasting away, yet inwardly we are being renewed day by day. For our light and momentary troubles are achieving for us an eternal glory that far outweighs them all. So, we fix our eyes not on

what is seen, but on what is unseen, since what is seen is temporary, but what is unseen is eternal." Paul also discusses how he is not perfect, but has the goal of living a Christ-like life. In Philippians 3:12-16 Paul is discussing being made perfect in the Lord and states, "Not that I have already obtained all this, or have already arrived at my goal, but I press on to take hold of that for which Christ Jesus took hold of me. Brothers and sisters, I do not consider myself yet to have taken hold of it. But one thing I do: Forgetting what is behind and straining toward what is ahead. I press on toward the goal to win the prize for which God has called me heavenward in Christ Jesus." This Scripture illustrates the importance of seeking scientific assistance for PANDAS and doing all that a parent is capable of for their child, but not losing hope, because science is not the final answer in PANDAS healing, but God providing healing. Isaiah 65:24 says, "I will answer them before they even call to me. While they are still talking about their needs, I will go ahead and answer their prayers!"

The Bible states many times to keep hope and faith, and rest in God's power and glory. Galatians 5:22-23 says, "But the fruit of the Spirit is love, joy, peace, forbearance, kindness, goodness, faithfulness, gentleness and self-control." The Bible mentions the word "rest" 275 times. The Bible calls people to be at peace and rest and believe God's promises. In the book of John, Mary and Martha tell Jesus about Lazarus. The Bible states in John 11:6 that Jesus knew Lazarus was sick, but he loved Mary and Martha so he stayed where he was for two more days. When Jesus gets to Lazarus days later, Jesus tells them as stated in John 11:40, "Did I not tell you if you would only believe you would see the glory of God?" The Bible is teaching that God loves His people enough not to deliver them in their time, but in His time. The Bible promises us that all things will

work together for good, to rest, and to have faith. Matthew 17:20 says, “Truly I tell you, if you have faith as small as a mustard seed, you can say to this mountain, ‘Move from here to there,’ and it will move. Nothing will be impossible for you.” To believe God’s promises, families need to rest in faith for healing from PANDAS. If parents try to make things happen in their time and not God’s it will lead only to frustration and resentment. God does not call His people to be frustrated, he calls them to rest and have faith. Faith for PANDAS families is knowing God’s promises before they are evident in the circumstance. Parents love their children and want whole healing for them. Parents rely and believe in the promise in Philippians 1:6, “Being confident of this, that He who began a good work in you will carry it on to completion.”

Biblical Summary

During times of uncertainty when dealing with a PANDAS diagnosis of a child, parents must equip themselves with the armor of God to persevere through the disease to reach remission. In 2 Corinthians, Paul prays to have the thorn from his flesh removed on three different occasions, but God does not remove it and explains that it is beneficial to him. 2 Corinthians 12:7-9 states, “To keep me from becoming conceited because of these surpassingly great revelations, there was given me a thorn in my flesh, a messenger of Satan, to torment me. Three times I pleaded with the Lord to take it away from me. But he said to me, ‘My grace is sufficient for you, for my power is made perfect in weakness.’ Therefore, I will boast all the more gladly about my weaknesses, so that Christ's power may rest on me.” Parents must keep in mind in dealing with this illness that His power is made perfect in our weakness, such as the weakness of a child with an illness. Parents have to persevere for the sake of their children. John 20:29 says, “Blessed

are those who have not seen and yet believed." Although parents are rightfully discouraged, they must remember to put their faith in God and wait for His timing for healing. Hebrews 12:1 says, "And let us run with perseverance the race marked out for us."

Summary

In a study by Leon et al. (2018), at follow-up, 29 of the 33 participants were experiencing no or only subclinical OCD symptoms. Of the remaining 4 with clinically significant OCD symptoms, one child was currently experiencing a symptom exacerbation at the time of follow-up, one child had discontinued all treatments before all symptoms had resolved, and two children had persistent OCD and remained in treatment (Leon et al., 2018). In a study by Colvin et al. (2021) the cognitive, graphomotor, and psychosocial challenges PANDAS patients face were ongoing and significant academic difficulty and emotional, behavioral, and social concerns remained after symptom resolution.

In a retrospective study of 40 patients, Latimer et al. (2015) concluded that improvement with therapeutic plasma exchange was not associated with the duration of illness. In a study by Gruijter et al. (2021), a bidirectional relationship between puberty and autoimmune rheumatic disease was found. In a case study by Cross et al. (2021), the researchers conclude that after a span of 31 months of illness and treatment with antimicrobials and IVIG, the patient reached complete remission. A study by Gromark et al. (2021) found that although complete remission was rare, 85% of patients had greatly improved at 2 to 5 years follow-up. The aforementioned studies create a starting point for this study. Very little is known about the remission of PANDAS. This study will take a

qualitative approach to factors of remission in PANDAS, that could lead to future research detailing what treatments lead to remission and reduction of symptom exacerbations.

CHAPTER 3: RESEARCH METHOD

Overview

The purpose of this qualitative phenomenological case study was to explore parents' perceptions of factors contributing to the remission of PANDAS. In a retrospective study of 40 patients, Latimer et al. (2015) concluded that improvement with therapeutic plasma exchange was not associated with the duration of illness. In a study by Gruijter et al. (2021) a bidirectional relationship between puberty and autoimmune rheumatic disease was found. In a case study by Cross et al. (2021), the researchers conclude that after a span of 31 months of illness and treatment with antimicrobials and IVIG, the patient reached complete remission. A study by Lepri et al. (2019) concluded that infection-related relapses were observed in 167 out of 371 participants long-term. Mohammad and Dale (2018) concluded that the majority of PANS/PANDAS patients will have relapse, persistent OCD, and tics. Mohammad and Dale (2018) also conclude that in PANS/PANDAS patients the speed of recovery is typically rapid, whereas in other immune-mediated movement disorders, such as SC, can take months to years. Very little is known about the remission of PANDAS. Based on the studies by Latimer et al. (2015), Gruijter et al. (2021), Cross et al. (2021), Lepri et al. (2019), and Mohammad and Dale (2018), it seems the factors in PANDAS remission, as well as what typical remission and subsequent symptom exacerbations entails, is not clearly defined.

This study took a qualitative approach to parents' perceptions of factors in remission, in order to understand the lived experiences of PANDAS families and the journey to remission. This study investigated parent's perceptions on factors of remission in PANDAS. This study analyzed patterns related to age, severity of illness, treatment

methods, and symptom exacerbations as factors of remission in PANDAS. Studies related to long-term outcomes of PANDAS, effective treatments, and remission management are scarce and/or inconclusive. This study aimed to discover patterns leading to remission and can guide future research on exploration of factors of remission in PANDAS and will serve as a road map for parents of children recently diagnosed with PANDAS.

Purpose of the Study

The purpose of this qualitative phenomenological case study was to explore parents' perceptions of factors contributing to the remission of PANDAS. This study aimed to discover patterns in reaching PANDAS remission related to age, severity of illness, treatment methods, and symptom exacerbations. The study used a 16-question original survey on Qualtrics related to parents' perceptions of factors of remission in PANDAS. Findings from this study can be used in future research to discover cause and effect relationships between treatment methods, age, and symptom severity to better guide treatment protocols in the future.

Research Questions

RQ1: According to parents' perceptions, which treatment is most effective in achieving remission?

RQ2: According to parents' perceptions, how long does achieving remission take?

RQ3: According to parents' perceptions, is length of PANDAS illness prior to receiving diagnosis and treatment related to achieving remission?

RQ4: According to parents' perceptions, is severity of PANDAS symptoms related to achieving remission?

RQ5: According to parents' perceptions, is age of PANDAS patient at symptom onset related to achieving remission?

RQ6: According to parents' perceptions, is presence of puberty related to PANDAS symptoms?

RQ7: According to parents' perceptions, are symptom flares experienced after achieving remission?

RQ8: According to parents' perceptions, is gender related to presence of remission?

RQ9: According to parents' perceptions, what is the most effective treatment for remission maintenance?

Research Design

The goal of this study was to better understand the factors involved in remission for PANDAS patients according to parents' perceptions. Therefore, this research was best suited for a qualitative study to allow for the understanding of the lived experience of PANDAS families remission experiences rather than testing cause and effect relationships. According to Creswell and Poth (2018, p. 8), qualitative research begins with an assumption and uses interpretive and theoretical frameworks to inform the study to address research problems by addressing a group with a human problem, in this case, PANDAS remission. In order to study the problem, the researcher takes a qualitative approach in order to find patterns or themes. The findings of the study include a complex description and interpretation of the problem and its contribution to the literature (Cresswell & Poth, 2018, p. 8). Mack et al. (2005) describes qualitative research as

seeking to explore phenomena, using more flexible instruments, in order to describe and explain relationships.

As a methodological approach, phenomenology allows for the examination of the lived experience of the journey to remission in PANDAS. According to Cresswell and Poth (2018) phenomenology has an emphasis on a single concept or idea; in this study, this concept is remission. This study aims to understand parents' perceptions of factors of remission from parents of children diagnosed with PANDAS. This study aimed to understand parents' perceptions of remission from parents of children diagnosed with PANDAS.

Data in this study were analyzed using a transcendental phenomenological approach. Creswell and Poth (2018) describe phenomenology as describing the personal experiences with the phenomenon under study. The phenomenon seeking to be better understood in this study is the process of remission in PANDAS. Phenomenology creates a description of what the participants in the study experienced, how the experience happened, and aims to capture the essence of the phenomenon (Creswell & Poth, 2018, p. 201). By using a transcendental phenomenological approach, the researcher is able to find themes and patterns in the phenomena under investigation. In a phenomenological case study, reality needs to be interpreted. In a phenomenological approach, the researcher is able to use epoche, or bracketing, to account for their own experience. By using epoche, the researcher acknowledges and discusses their experience with the phenomena, but puts that aside in order to try to better understand the experience of the participants (Cresswell & Poth, 2018). Hardy (2018) describes etic as the outsider's perspective, and it is achieved by examining and interpreting data through a psychological lens in which the

researcher finds helpful to bring an understanding of the research questions. Hardy (2018) describes emic as the insider's perspective, which takes a pragmatic approach to help the researcher shape the varied nature of the explanations from the study. The pragmatism paradigm asserts that the best method is one that solves problems. The transcendental phenomenological approach allows for flexibility in the study so that the researcher can modify guidelines to fit their research objectives (Creswell & Poth, 2018).

Case Study Design

This study is classified as a multiple series case study. This study used a priori critical case sampling, which allowed for logical generalizations of remission experiences and provided maximum application of information to other cases of PANDAS families (Cresswell & Poth, 2018, p. 159). It was difficult to estimate an appropriate sample size of remission experiences since there is limited literature related to long-term PANDAS outcomes (Kovacevic et al., 2015; Latimer et al., 2015; Leon et al., 2018). In previous studies regarding treatment outcomes, researchers have conducted single case studies or have sample sizes of 40 participants or less (Brown et al., 2017; Calaprice et al., 2018; Demesh et al., 2015; Kovacevic et al., 2015; Latimer et al., 2015; Leon et al., 2018). Calaprice et al. (2018) is the only large-scale treatment outcome study that could be located. Calaprice et al. (2018) conducted a retrospective study of 698 participants and asked questions related to treatment experiences. The study by Calaprice et al. (2018) is similar to this study proposal; however, the study by Calaprice et al. (2018) includes all PANS diagnoses and is not specific to only PANDAS.

There are two types of phenomenology, Hermeneutic and transcendental (Cresswell & Poth, 2018). This study used transcendental phenomenology, which is

oriented toward the description of the experience of the participants. The researcher uses the concept of epoche in order set aside their own experiences. The researcher bracketed herself out of the study by discussing her own relationship with PANDAS which allowed for a better understanding of participant experiences.

This study used critical case sampling, which allows for logical generalizations of remission experiences and provides maximum application of information to other cases of PANDAS families who have not yet reached remission (Cresswell & Poth, 2018, p. 159). This study took a direct interpretation approach, which allowed the researcher to look at the instance of remission in PANDAS and extrapolate the data in more meaningful ways (Cresswell & Poth, 2018, p. 206). This study used Wolcott's (1994) approach to validation with the premise that in this study validity of a survey tool would neither guide nor inform the qualitative research, as the goal was to gain a better understanding of PANDAS remission (Cresswell & Poth, 2018, p. 255). Wolcott (1994) states that understanding is better than validity, and the goal of this study was to gain better understanding of PANDAS remission (Cresswell & Poth, 2018, p. 255).

The sampling process and emergence of patterns in data analysis allows generalizations of information that can be used as building blocks in future research. This study included 16 survey questions on Qualtrics to be answered by parents of children diagnosed with PANDAS (See Appendix A).

Participants

Participants were at least 18 years old, with English as their primary language, and the parent of a child diagnosed with PANDAS from a medical doctor. Parents of children diagnosed with PANDAS were identified through Facebook PANDAS support

groups and the National Institute of Mental Health Outreach Partnership Program Aspire PANS/PANDAS newsletter. Exclusion criteria included lack of PANDAS diagnosis from a medical doctor, being under 18 years of age, or not being the parent of a child with PANDAS. The Facebook recruitment took place using a social media invitation to participate in a 16 question Qualtrics survey (See Appendix B). Following the link on the Facebook post redirected participants to the Qualtrics survey introduction and informed consent (See Appendix D). The Aspire newsletter recruitment took place using an invitation to participate in a 16 question Qualtrics survey (See Appendix B). Following a link in their email newsletter redirected participants to the Qualtrics survey introduction and informed consent (See Appendix D).

Facebook and Aspire newsletter administrators were contacted upon IRB approval of this study in order to gain permission for group participation in the study. Administrators were sent a message by the researcher upon IRB approval (See Appendix C). Once approval was granted, the group administrator either published the survey recruitment on their group page or granted the researcher permission to post the recruitment on the Facebook page or newsletter (See Appendix B).

The first page of the survey was the informed consent and introduction (See Appendix D). After providing consent in the first three questions, the participant was directed into the survey (See Appendix A). The Facebook group permissions were obtained from PANDAS-Pediatric Autoimmune Neuropsychiatric Disorder Associated w/Strep, PANDAS Parents, STL/Midwest PANDAS Support. Permission was requested but not granted from the Facebook group PARENTS OF CHILDREN WITH PANDAS/PANS/LYME/TICK-BORNE DISEASES. The administrators responded

without permission stating that because this study is only examining PANDAS and not PANS, they did not think it would appeal to their group members. Permission was also requested and received from the Aspire administrator. Aspire PANS/PANDAS is a national outreach partnership program through the National Institute of Mental Health. Aspire sends a monthly electronic newsletter to subscribers who have input their information on their website in order to receive the monthly newsletter. This information is not visible to the public.

PANDAS Facebook support groups serve as a social media resource for caregivers of children with PANDAS. These networks collaborate with experts, build public awareness, and serve as a resource and support to those providing care to PANDAS patients. The Aspire network states that the goal of the newsletter is to keep the community up to date with PANS/PANDAS news and information.

Inclusion criteria of participants included an official PANDAS diagnosis from a medical doctor, English as primary language, and being the legal parent of a child with PANDAS. Cresswell and Poth (2018) note that phenomenological study sample sizes can range from 1 to 325. This study was a multi-series case study with an aim to understand similarities and differences of factors in remission from PANDAS parent perspectives. A sample size of a minimum of 50 respondents of the questions allowed for logical generalizations and themes to emerge from the closed-ended data, and this seemed a logical sample size due to prior studies related to PANDAS outcomes (Brown et al., 2017; Calaprice et al., 2018; Kovacevic et al., 2015; Latimer et al., 2015; Leon et al., 2018;).

Study Procedures

The 16-question survey in this study is original and specifically designed for this study. Since no previous studies involving parental perceptions of PANDAS remission could be located, it was necessary to create an original survey for this study. Digital platforms for symptom tracking in PANS/PANDAS are being studied (Harris et al., 2021). These platforms are new and require further research. The information obtained from these platforms will be a helpful tool if released for data extrapolation in future studies.

Upon IRB approval, the Facebook group and Aspire program administrators were sent messages requesting the survey invitation be posted to the Facebook group and monthly electronic Aspire newsletter (See Appendix C). Upon receiving permission, the survey invitation to participate was posted on the Facebook group pages and included in the Aspire email newsletter. The survey invitation included the link to the Qualtrics survey. Respondents clicking the link on the Facebook page or in the electronic newsletter directed them to the survey informed consent and introduction, which includes the process, procedures, inclusion criteria, and informed consent with researcher contact information (See Appendix D).

Upon consent, participants were directed to the survey page for completion (See Appendix A). Surveys were completed anonymously, with no identifying information of participants being collected. Data was stored on a password-protected computer using multi-factor authentication. Only the researcher has access to the data. Participants could choose not to participate at any time prior to submitting the survey by closing their internet browser. The informed consent was the introduction to the survey, and

participants could choose not to participate by closing their internet browser. Consent to participate directed participants to begin the survey on the following page. The first three questions on the survey are the inclusion criteria questions. Answering "no" to any of the inclusion questions automatically redirected the respondent to the end of the survey using the Skip-Logic feature in Qualtrics. There is no direct risk or benefit to participants. The benefit to society will be increased research on PANDAS.

Instrumentation and Measurement

This study used Wolcott's (1994) approach to validation with the premise that in this study validity of a survey tool would neither guide nor inform the qualitative research, as the goal was to gain a better understanding of PANDAS remission (Cresswell & Poth, 2018, p. 255). At the time of this study, no valid instrument exists for the measurement of PANDAS remission, nor has the definition of remission in PANDAS been clearly defined. Wolcott (1994) states that understanding is better than validity, and the goal of this study was to gain better understanding of PANDAS remission (Cresswell & Poth, 2018, p. 255). The sampling process and emergence of patterns in data analysis allow generalizations of information that can be used as building blocks in future research. The 16-question survey in this study was original and specifically designed for this study. Since no previous studies involving parental perceptions of PANDAS remission could be located, it was necessary to create an original survey for this study. Other studies of remission in other diseases have used the DAS28 to measure remission; however, these studies state that further defining of remission using this tool is needed (Felson, 2011; Gul et al., 2021; Wilhelm et al., 2016).

Understanding the thoughts, feelings, and experience of the participants is the goal of the study; however, the questions allow for certain research questions to be answered. Survey responses were anonymous, and no identifying information was requested from survey participants. The informed consent was the introduction to the survey, and participants could choose not to participate or consent by closing their internet browser. Consent to participate directed participants to begin the survey on the following page. The first three questions on the survey were the inclusion criteria questions. Answering "no" to any of the inclusion questions automatically redirected the respondent to the end of the survey using the Skip-Logic feature in Qualtrics. Records are kept under the login of only the author of this study on the Qualtrics platform and will be retained for a minimum of three years per IRB regulations. Clicking the survey link on the Facebook group post or newsletter invitation directed participants to a consent form that details the purpose and procedures of the study as well as researcher contact information and informed consent before the decision to participate (See Appendix D).

Data Analysis

The data gathered from the survey were analyzed and checked for emerging patterns using IBM SPSS Statistics 28. Cresswell and Poth (2018) recommend conducting cross-case theme analysis in order to examine if patterns or themes emerge. The survey responses were analyzed using Pearson and Point Biserial correlations and frequency distributions to analyze generalizable patterns using SPSS software.

Using the bivariate analysis feature in SPSS, variables of the survey related to remission were entered and compared using IBM SPSS Statistics 28 software. Bivariate correlations are generally used to describe two or more phenomena happening together,

which can lead to future cause-and-effect studies to see if the phenomena occurring together provides evidence of causation. A bivariate point biserial correlation was conducted on age at onset and presence of remission, symptom severity and presence of remission, length of illness and presence of remission, and gender and presence of remission.

Using the frequency distribution feature in IBM SPSS Statistics 28, frequency distributions were used to determine frequencies of males and females diagnosed with PANDAS, frequency of severity of disorder, frequency of what parents consider most effective treatments for reaching remission, frequency of what parents consider most effective treatments for remission maintenance, frequency of symptoms of PANDAS after puberty, and the frequency of symptom flares in remission.

Delimitations, Assumptions, and Limitations

Limitations of this study are the parents' perceptions, whether it is mother or father completing the survey, as mothers and fathers could have different perceptions of the PANDAS experience. Another limitation could be recall bias, as parents may not clearly remember lengths of time or symptom severity. Additional limitations include conservatism, regressive bias, or consistency bias, as parents may not remember exactly how much a treatment helped or may not remember how bad or good symptoms or treatment effects were at a particular time.

A delimitation of this study is that it will not address specific brands, doses, or length of time various treatments were used, as many PANDAS patients use more than one treatment. Another delimitation of this study is lack of clinical confirmation of diagnosis. Another delimitation of this study is the use of an original survey rather than

an instrument that has been sufficiently tested for reliability and validity. PANDAS remission literature is scarce, therefore there is not enough published research to employ quantitative experimental studies to determine true clinical remission factors at this time. Therefore, results of this study are limited by parental perceptions, but will serve as a basis for future research using quantitative techniques.

An assumption of this study is the understanding of the concept of remission. This word could have different meaning to different audiences related to chronic conditions. In other studies, related to remission in lupus and rheumatoid arthritis, differences in the definition of remission include remission being defined as no clinical signs of disease activity or disease activity at a low enough level that the symptoms are no longer troublesome to the patient (Wilhelm et al., 2016). Remission in PANDAS will need to be defined to address disease activity levels and if remission includes maintenance treatment. The assumption of the researcher is that remission is defined as no longer experiencing PANDAS symptoms, and does not specify remission as remission without treatment or remission while on treatment. Wilhelm et al. (2016) states that the respondents of a study created variance in the time it takes to reach remission because of the participant's definition of remission. Therefore, having a clear definition of PANDAS remission in the future will be important in future studies.

Summary

The purpose of this qualitative phenomenological case study was to explore parents' perceptions of factors contributing to the remission of PANDAS and examine if age, symptom severity, and length of illness are related to remission. Future research should be aimed at creating practitioner awareness to lead to more timely and appropriate

treatment of patients, and exploring which treatment methods are most effective in reaching remission of PANDAS. Future studies related to remission should include a clear definition of remission in PANDAS, and an instrument that can be used to measure the presence of remission in PANDAS patients.

CHAPTER 4: RESULTS

Overview

The purpose of this qualitative phenomenological case study was to explore parents' perceptions of factors related to PANDAS remission. Parents of children diagnosed with PANDAS were recruited through Facebook PANDAS support groups and the National Institute of Mental Health Outreach Partnership Program Aspire PANS/PANDAS newsletter and followed a link to a Qualtrics survey containing 16 questions related to their perception of remission. Inclusion criteria included an official diagnosis of PANDAS from a medical doctor, being the legal parent or guardian of the PANDAS patient, with English as the primary language. This study sets a foundation for future studies to explore why and how various treatments are more or less effective, will serve as a starting point for future experimental studies on treatment methods, and can serve as a roadmap for families with a recent PANDAS diagnosis.

Descriptive Results

This study used critical case sampling, which allows for logical generalizations of remission experiences and provides maximum application of information to other cases of PANDAS families that have not yet reached remission (Cresswell & Poth, 2018, p. 159). This study took a direct interpretation approach, which allowed the researcher to look at the instance of remission in PANDAS and extrapolate the data in more meaningful ways (Cresswell & Poth, 2018, p. 206). This study used Wolcott's (1994) approach to validation with the premise that in this study validity of a survey tool would neither guide nor inform the qualitative research, as the goal was to gain a better understanding of PANDAS remission (Cresswell & Poth, 2018, p. 255). Wolcott (1994)

states that understanding is better than validity, and the goal of this study was to gain better understanding of PANDAS remission (Cresswell & Poth, 2018, p. 255).

The sampling process and emergence of patterns in data analysis allows generalizations of information that can be used as building blocks in future research. This study included 16 survey questions on Qualtrics to be answered by parents of children diagnosed with PANDAS.

The data gathered from the survey was analyzed and checked for emerging patterns using IBM SPSS Statistics 28. Cresswell and Poth (2018) recommend conducting cross-case theme analysis in order to examine if patterns or themes emerge. The survey responses were analyzed using Pearson and Point Biserial correlations and frequency distributions to analyze generalizable patterns using SPSS software. Pearson's r is a correlation used when both variables are scale, and point biserial correlations are used when one variable is scale and one is nominal and dichotomous. This study used a .05 level of significance for two-tailed tests, with a critical value of the Pearson r of .2050.

Using the bivariate analysis feature in SPSS, variables of the survey related to the presence of remission were entered and compared using IBM SPSS Statistics 28 software. Bivariate correlations are generally used to describe two or more phenomena happening together. A bivariate point biserial correlation was conducted on age at onset and presence of remission, symptom severity and presence of remission, length of illness before diagnosis and presence of remission, and gender and presence of remission.

Using the frequency distribution feature in IBM SPSS Statistics 28, frequency distributions were used to determine frequencies of males and females diagnosed with

PANDAS, frequency of severity of disease, frequency of what parents consider most effective treatments for reaching remission, frequency of what parents consider most effective treatments for remission maintenance, frequency of symptoms of PANDAS after puberty, frequency of symptom flares in remission, and frequency of how long reaching remission takes.

Participants

A total of 87 parents participated in the study. Participants were parents of children diagnosed with PANDAS. The parents answered questions about their children. The mean age of PANDAS onset was 7.1 years (range 1-18, SD=3.56) and current mean age is 13.4 years (range 4-30). Participants were 67.8% male and 32.2% female (n=87, 59 male, 28 female). Mean age at beginning of PANDAS treatment is 9.0 years (range 4-28, SD=4.18). Mean age at PANDAS onset for males is 6.5 years (n=59) and mean age at PANDAS onset for females is 8.3 years (n=28). Mean age at PANDAS diagnosis and treatment for males is 8.41 years (n=59, SD=3.67). Mean age at PANDAS diagnosis and treatment for females is 10.32 (n=28, SD=4.93). The mean length of time between symptom onset and receiving PANDAS diagnosis to begin PANDAS treatment is 23.75 months (n=87, range 0-180).

Evidence of Quality

Mack et al., (2005) describes qualitative research as seeking to explore phenomena using more flexible instruments in order to describe and explain relationships. Evidence of quality can be viewed through a sampling of survey responses (See Appendix E). This study used an original survey to explore parents' perceptions of factors of remission in PANDAS. The survey was approved by the Institutional Review

Board of Liberty University and permissions from group administrators for advertisement of the study were granted (See Appendix B). For assurance of research quality and timeliness, 80% of sources cited in this study were current within the last five years. Rallis and Rossman (2012, p. 18) state that the goal of qualitative research is learning by transforming data into information that can be used. Phenomenology creates a description of what the participants in the study experienced and how the experience happened, and it aims to capture the essence of the phenomenon (Creswell & Poth, 2018, p. 201). The researcher transformed the data from the study into information that can guide areas for future PANDAS research. Qualitative data generally uses codes as a method of organizing data. Codes for this study are explained in notation format below the respective tables.

Study Findings

The purpose of this qualitative phenomenological case study was to explore parents' perceptions of factors related to PANDAS remission. Parents of children diagnosed with PANDAS were recruited through Facebook PANDAS support groups and followed a link to a Qualtrics survey containing 16 questions related to their perception of remission. Inclusion criteria included an official diagnosis of PANDAS from a medical doctor, being the legal parent or guardian of the PANDAS patient, with English as the primary language.

The goal of this study was to better understand the factors involved in remission for PANDAS patients according to parents' perceptions. Therefore, this research was best suited for a qualitative study to allow for the understanding of the lived experience of PANDAS families remission experiences rather than testing cause and effect

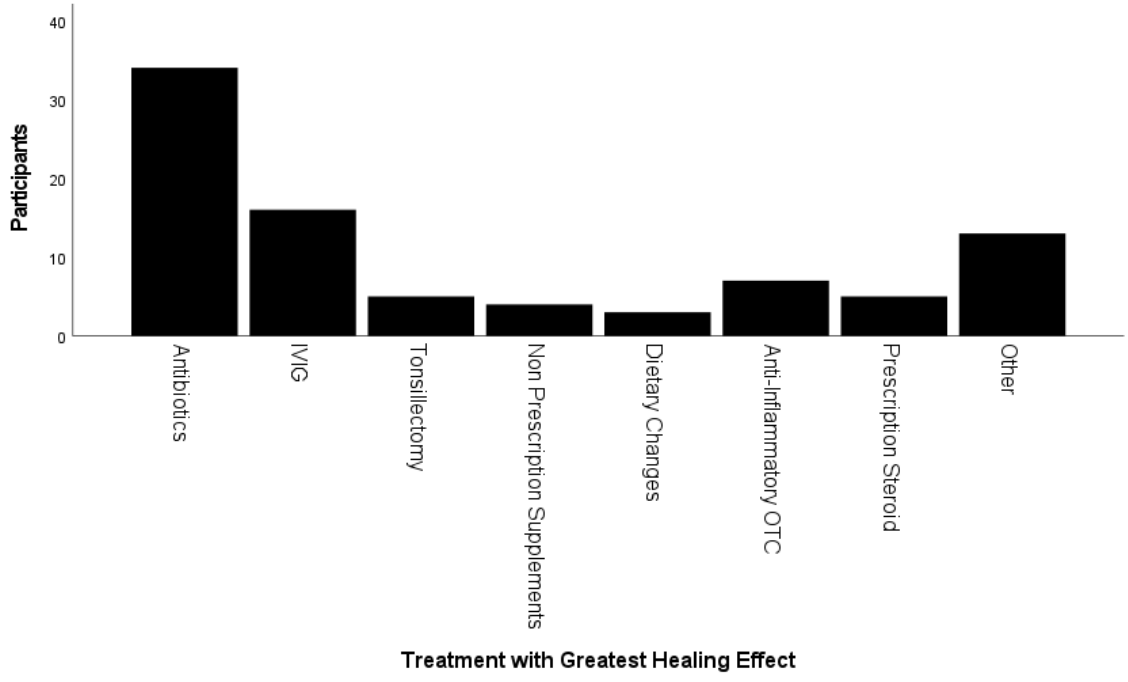
relationships. According to Creswell and Poth (2018, p. 8), qualitative research begins with an assumption and uses interpretive and theoretical frameworks to inform the study to address research problems by addressing a group with a human problem, in this case, PANDAS remission.

RQ1: According to parents' perceptions, which treatment is most effective in achieving remission?

Using the frequency distribution feature in SPSS, a frequency distribution was used to examine frequency of parent-reported effective treatments for achieving remission. According to parents (n=87), antibiotics had the single greatest healing effect (n=34, 39.1%). Followed by IVIG/Therapeutic Plasma Exchange (n=16, 18.4%), then undescribed "other" (n=13, 14.9%), then anti-inflammatory over-the-counter drugs (n=7, 8.0%), tonsillectomy and prescription steroid ranked equally, (tonsillectomy, n=5, 5.7%, prescription steroid, n=5, 5.7%), followed by non-prescription supplements (n=4, 4.6%), Q6 Which treatment had the greatest healing effect, and last dietary changes (n=3, 3.4%). See Figure 1.

Figure 1

Treatment with Greatest Healing Effect

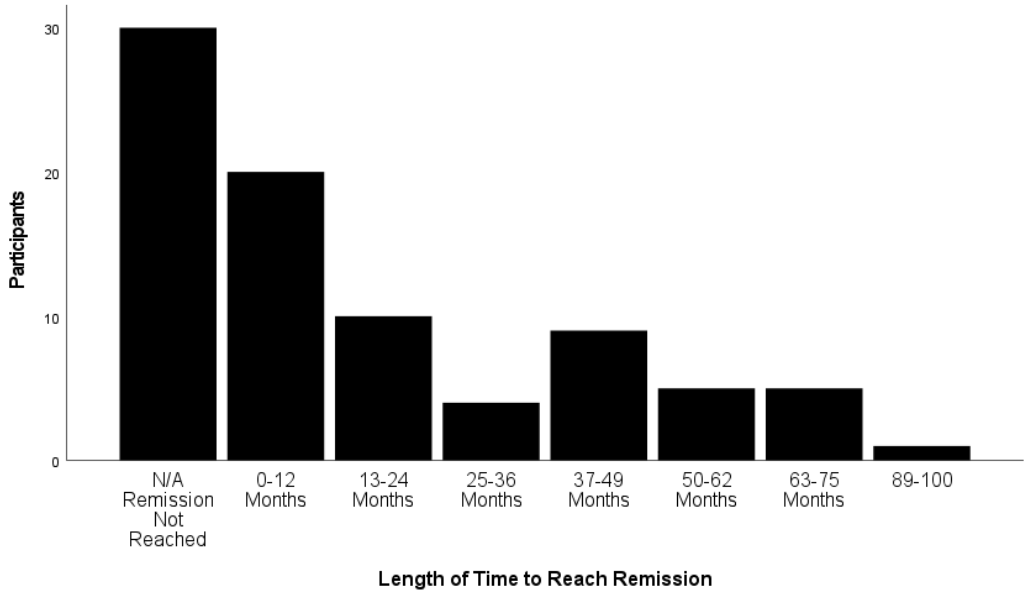


RQ2: According to parents' perceptions, how long does achieving remission take?

Using the frequency distribution feature in SPSS, a frequency distribution was used to examine frequency of parent-reported length of time (in months) for remission to be reached. This study revealed that, according to parents' perceptions, the mean months to remission was 18.64 (n=84). See Figure 2. Of the 87 survey participants, 3 had missing data, 54 stated they had achieved remission and 30 stated they had not reached remission.

Figure 2

Length of Time to Reach Remission



RQ3: According to parents' perceptions, is length of PANDAS illness prior to receiving diagnosis and treatment related to presence of remission?

Using the bivariate correlation feature in SPSS, a Point Biserial correlation was used to examine the parent-reported length of time (in months) that children were undiagnosed/untreated compared to presence of remission. The findings of this study indicate that the length of PANDAS illness prior to receiving diagnosis and treatment is not related to achieving remission. See Figure 3. A Point Biserial Correlation revealed there is not a statistically significant relationship between the length of time of illness before diagnosis and treatment and presence of remission, $r(85) = 0.03$, $p > .05$ (two-tailed). Using the bivariate correlation feature in SPSS, a Pearson's r correlation was used to examine the parent-reported length of time (in months) before receiving treatment/diagnosis and the length of time (in months) to reach remission. A Pearson's r Correlation revealed there is not a statistically significant relationship between the length of time before receiving diagnosis and treatment and the length of time to reach remission, $r(87) = .11$, $p>.05$ (two-tailed). See Figure 4.

Figure 3

Length of Time to Receive Diagnosis and Presence of Remission

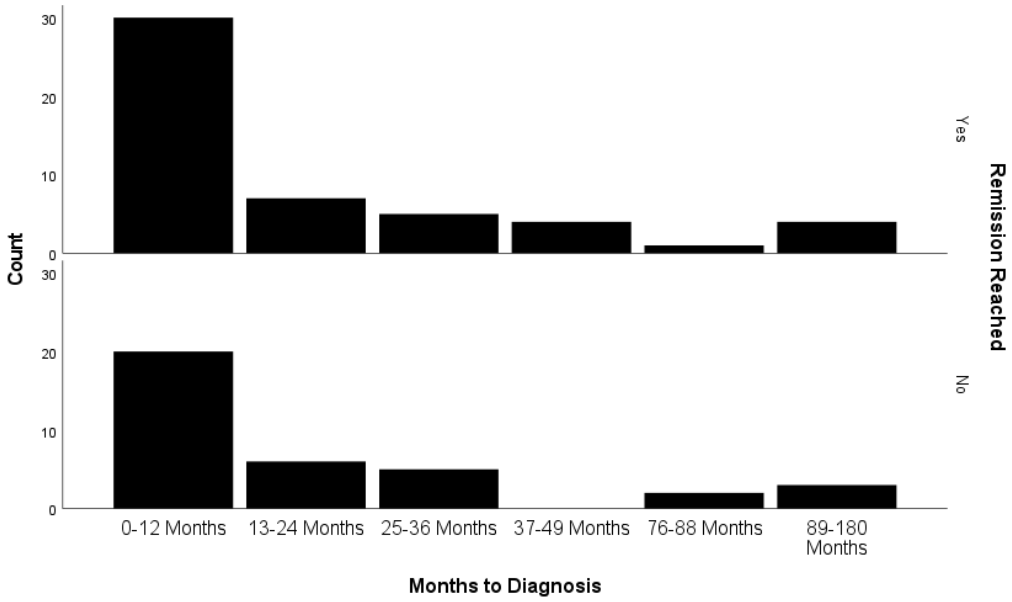
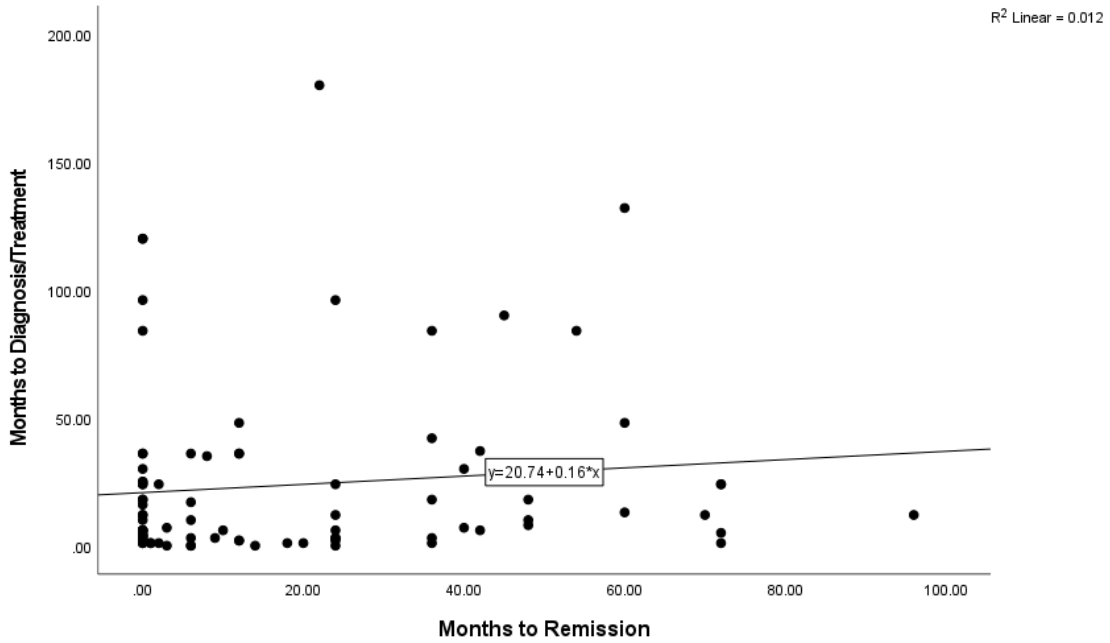


Figure 4

Months to Receive Diagnosis and Treatment and Months to Remission



RQ4: According to parents' perceptions, is severity of PANDAS symptoms related to achieving remission?

Using the frequency distribution feature in SPSS, a frequency distribution was used to examine parent-reported symptom severity. According to parents' perceptions, 52.9% of cases are severe (n=46), 40.2% of cases are reported as moderate (n=35), and 6.9% are reported as mild (n=6). See Figure 5. Using the bivariate correlation feature in SPSS, a Point Biserial correlation was used to examine the parent-reported PANDAS symptom severity and presence of remission. The results of this study indicate the severity of PANDAS symptoms are not related to presence of remission. See Figure 6. A Point Biserial correlation revealed there is not a statistically significant relationship between symptom severity and length of time to reach remission, $r(85) = .02$, $p > .05$ (two-tailed).

Figure 5

Parents' Perception of PANDAS Symptom Severity

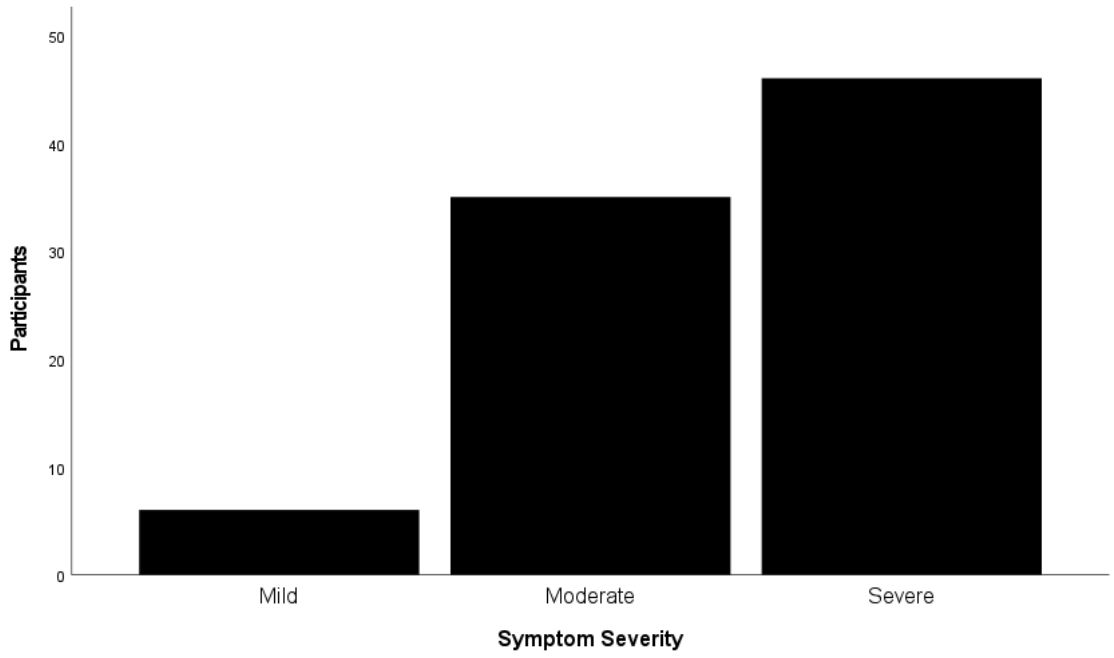
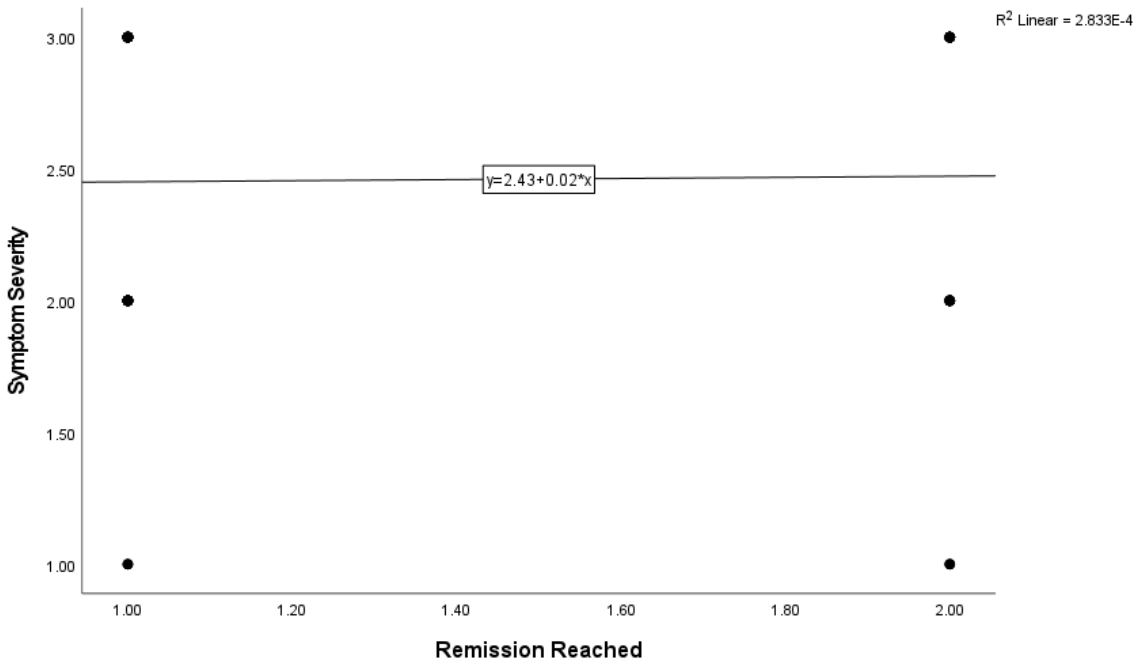


Figure 6

Symptom Severity and Presence of Remission



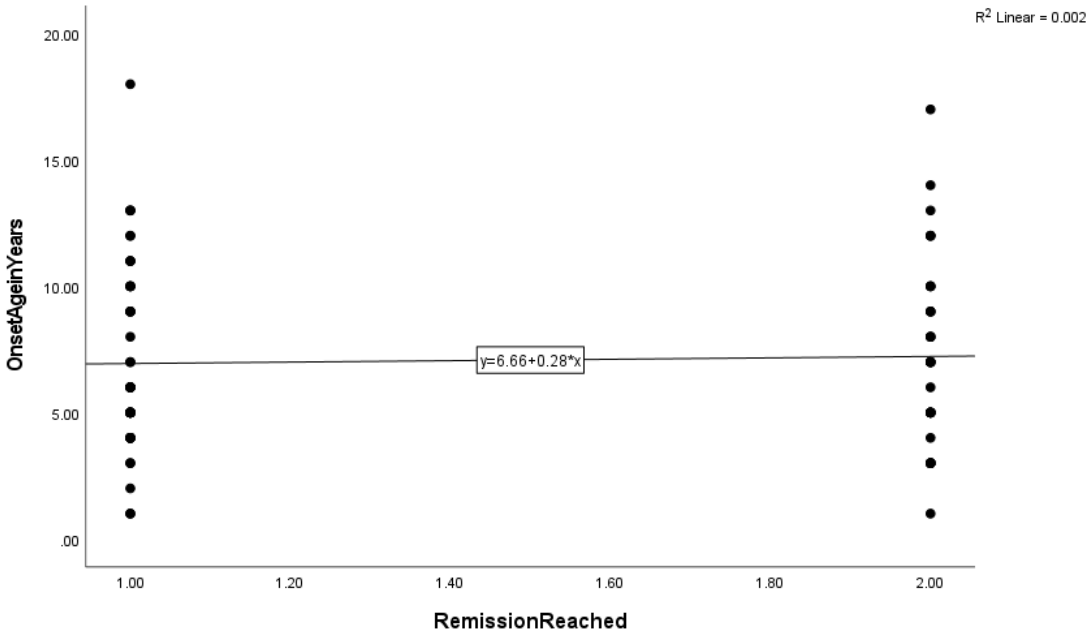
Note. Remission reached coded 1 (yes) and 2 (no).

RQ5: According to parents' perceptions, is age of PANDAS patient at symptom onset related to achieving remission?

Using the bivariate correlation feature in SPSS, parent-reported age of PANDAS patient (in years) at PANDAS symptom onset and presence of remission was examined. A Point Biserial correlation revealed there is not a statistically significant relationship between age at onset and presence of remission, r (85) = 0.04, p> .05 (two-tailed). See Figure 7.

Figure 7

PANDAS Onset Age and Presence of Remission



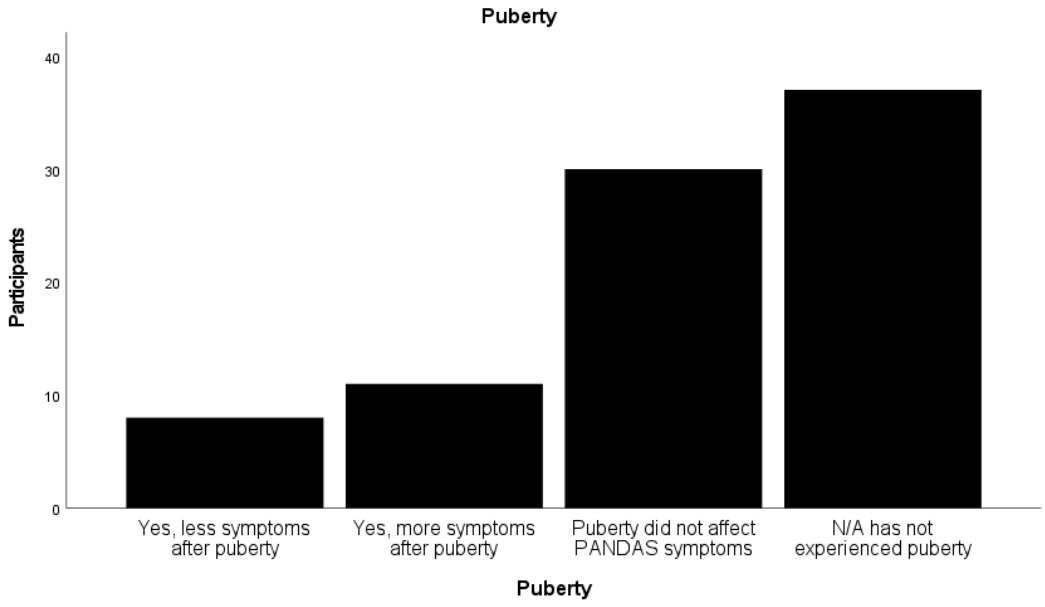
Note. Remission reached is coded 1 (yes) and 2 (no).

RQ6: According to parents' perceptions, is presence of puberty related to PANDAS symptoms?

Using the frequency distribution feature in SPSS, parent-reported presence of puberty's effect on PANDAS symptoms was examined. According to parents (n=86), 37 of the children have not yet experienced puberty. Of the remaining, (n=49), 8 indicated less PANDAS symptoms after puberty, 11 indicated more PANDAS symptoms after puberty, and 30 indicated puberty did not have an effect on PANDAS symptoms. See Figure 8.

Figure 8

Puberty and Effect on PANDAS Symptoms

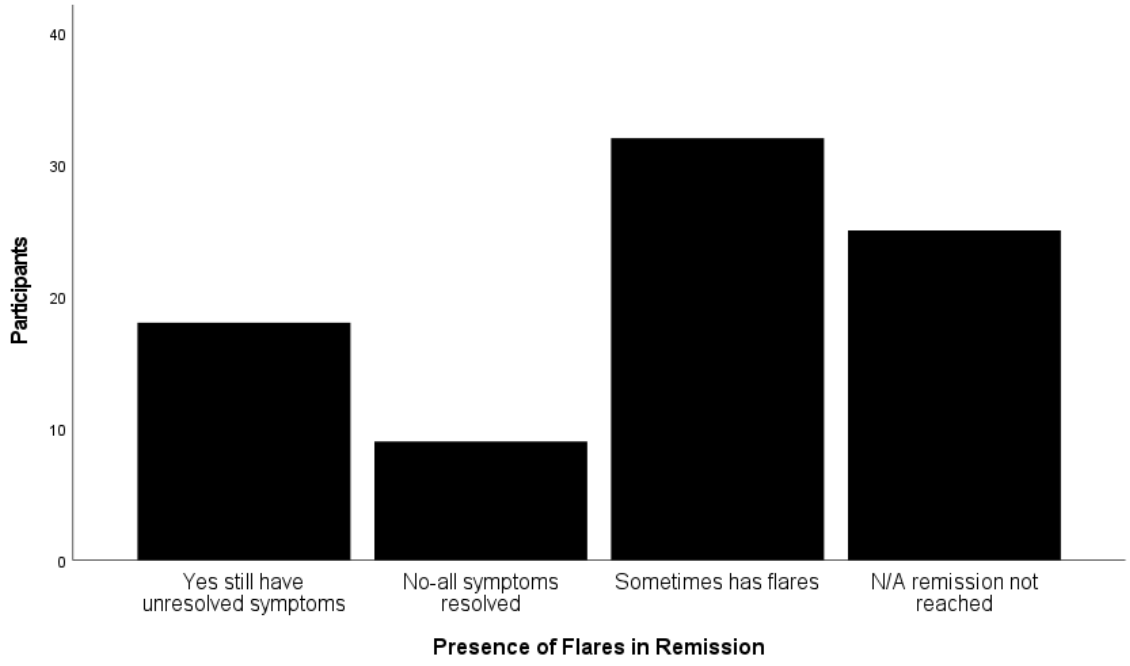


RQ7: According to parents' perceptions, are symptom flares experienced after achieving remission?

Using the frequency distribution feature of SPSS, a frequency distribution was used to examine parent-reported PANDAS symptom flares experienced after remission had been achieved. According to parents' perceptions (n=84), 32 stated there are still symptom flares in remission, 9 indicated all symptoms had resolved, 18 said they have symptoms that have never resolved while in remission, and 25 parents indicated they have not yet reached remission. See Figure 9.

Figure 9

Symptom Flares Experienced in Remission

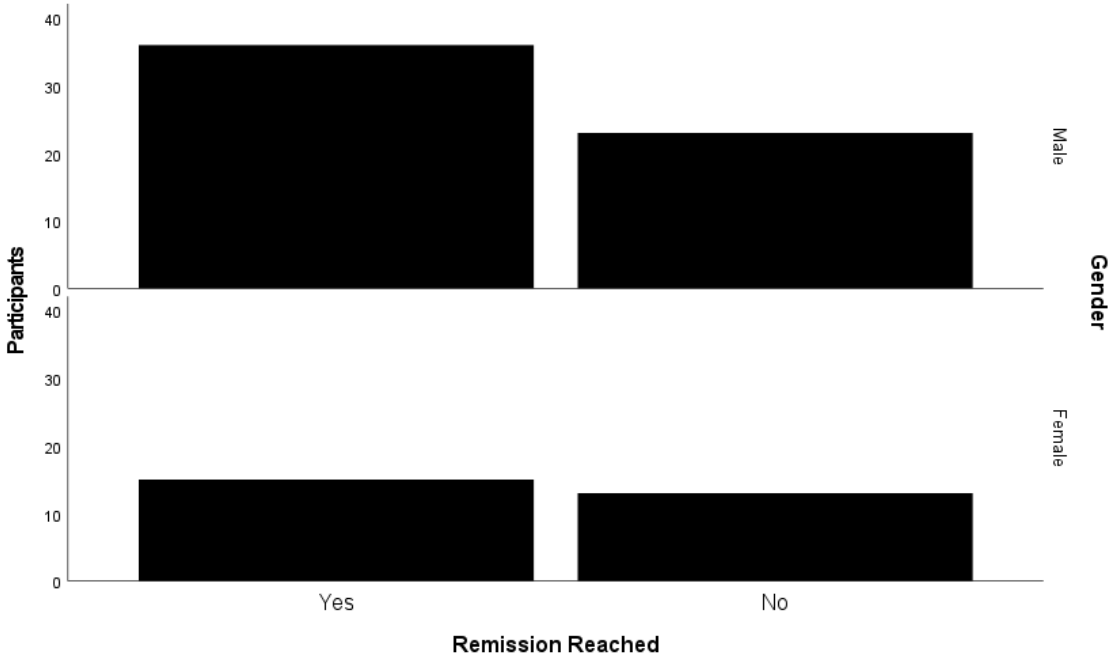


RQ8: According to parents' perceptions, is gender related to presence of remission?

Participants were 67.8% male and 32.2% female (n=87, 59 male, 28 female). Mean age at beginning of PANDAS treatment is 9.0 years (range 4-28, SD=4.18). Mean age at PANDAS onset for males is 6.5 years (n=59) and mean age at PANDAS onset for females is 8.3 years (n=28). Mean age at PANDAS diagnosis and treatment for males is 8.41 years (n=59, SD=3.67). Mean age at PANDAS diagnosis and treatment for females is 10.32 (n=28, SD=4.93). Using the bivariate correlation feature in SPSS, gender was compared to presence of remission. This study did not reveal a statistically significant relationship between gender and presence of remission, r (85) = .07, p > .05 (two-tailed). See Figure 10.

Figure 10

Presence of Remission and Gender



RQ9: According to parents' perceptions, what is the most effective treatment for remission maintenance?

Using the frequency distribution feature in SPSS, parent-reported most effective treatments for remission maintenance were compared. This study revealed that parents (n=87) consider prescription drugs most effective for remission maintenance, (n=34), followed by over-the-counter supplements or lifestyle changes to maintain remission (n=20), followed by no maintenance drugs of any kind required (n=8). Of the 87 parents surveyed, 25 indicated they had not yet reached remission. See Table 2.

Table 2

Parents' Perception of Most Effective Treatment for Remission Maintenance

RemissionMaintenance

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Yes, RX Meds used for maintenance	34	39.1	39.1	39.1
	Yes, OTC or lifestyle changes used for maintenance	20	23.0	23.0	62.1
	No maintenance meds used	8	9.2	9.2	71.3
	N/A Remission not reached	25	28.7	28.7	100.0
	Total	87	100.0	100.0	

Summary

The purpose of this study was to explore parents' perceptions related to factors of remission in PANDAS. Findings from this study are supportive of a previous study by Latimer et al. (2015) that length of illness is not related to presence of remission. This study is also supportive of prior research that PANDAS occurs more in males than females, generally with onset at age 6-8 years (Kovacevic et al., 2015; Swedo et al., 2015). This study also found that the mean length of time children were misdiagnosed or undiagnosed from symptom onset to beginning PANDAS treatment was 23.75 months (n=87). This study did not find statistically significant correlations between PANDAS symptoms, age, and severity related to remission. This study found that while in remission (n=59), the majority of children, 85%, still have PANDAS symptoms (n=50).

This study found that parents attribute antibiotics to the greatest PANDAS healing treatment effect (n=34) and IVIG as the second most important healing treatment (n=16). The findings of this study highlight the need for increased practitioner and community awareness of PANDAS diagnosis and treatment methods as well as future research needed to better understand PANDAS remission and treatments that could lead to lasting remission.

CHAPTER 5: DISCUSSION

Overview

The purpose of this qualitative phenomenological case study was to explore parents' perceptions of factors contributing to the remission of PANDAS. This study aimed to discover patterns in reaching PANDAS remission related to age, severity of illness, treatment methods, and symptom exacerbations. The study used a 16-question original survey on Qualtrics related to parents' perceptions of factors of remission in PANDAS. Findings from this study can be used in future research to discover cause and effect relationships between treatment methods, age, and symptom severity to better guide treatment protocols in the future.

Summary of Findings

The purpose of this study was to explore parents' perceptions related to factors of remission in PANDAS. Findings from this study are supportive of a previous study by Latimer et al. (2015) that length of illness is not related to presence of remission. This study is also supportive of prior research that PANDAS occurs more in males than females, generally with onset at age 6-8 years (Kovacevic et al., 2015; Swedo et al., 2015). This study also found that the mean length of time children were misdiagnosed or undiagnosed from symptom onset to beginning PANDAS treatment was 23.75 months (n=87). This study did not find statistically significant correlations between PANDAS symptoms, age, and severity related to remission. This study found that while in remission (n=59), the majority of children, 85%, still have PANDAS symptoms (n=50).

This study found that parents attribute antibiotics to the greatest PANDAS healing treatment effect (n=34) and IVIG as the second most important healing treatment (n=16).

The findings of this study highlight the need for increased practitioner and community awareness of PANDAS diagnosis and treatment methods as well as future research needed to better understand PANDAS remission and treatments that could lead to lasting remission.

Discussion of Findings

The findings of this study are supportive of prior research indicating that length of illness does not appear to be related to remission (Latimer, 2015). The mean length of time children were ill with PANDAS symptoms before receiving diagnosis and treatment in this study was 23.75 months (n=87). LaRusso et al. (2022) discusses gaps in diagnosis and care due to logistics of medical coverage thus compromising children's health and development. LaRusso et al. (2022) states that patients with PANS/PANDAS often receive untimely care. Rea et al. (2021) noted that worsening school performance, increased anxiety, irritability, and aggressivity all increase with symptom exacerbations. This study is evidence of the need for increasing practitioner and community awareness for PANDAS for children to receive a timely diagnosis and adequate care to help children with PANDAS thrive.

There was not a significant relationship between age of PANDAS onset, length of PANDAS illness without treatment, PANDAS symptom severity, or gender and presence of remission. The findings of this study are supportive that PANDAS affects more males than females, and that the typical age of onset is between 6-8 years (Harris et al., 2021; Kovacevic et al., 2015; Swedo et al., 2015). This study did not find a significant relationship between presence of puberty and presence of remission. In a study by Gruijter et al. (2021) a bidirectional relationship between puberty and autoimmune

rheumatic disease was found. Further research can be conducted related to long-term outcomes after the presence of puberty and remission to see if any relationship exists between age, puberty, and PANDAS remission.

Another important element of this study is the parent-reported effective treatment methods, with antibiotics and IVIG/TPE being the highest ranked effective treatment methods by parents. These findings suggest the importance of increasing practitioner awareness and training to provide proper care to PANDAS children. Pandas Physicians Network currently gives recommendations on which antibiotics seem to be most helpful in treating PANDAS symptoms, but more research is needed to determine what dosing and length of treatment is needed to reach and maintain remission. In a study by Leon et al. (2018), 72% (n=33) of participants experienced at least one PANDAS symptom exacerbation within the 6-57 month period following IVIG. Additional research related to IVIG dosing and frequency is needed to determine prescription parameters that help to not only quickly reach but also maintain remission. A study by Cross et al. (2021) concluded in a case study that with treatment over 31 consecutive months using various antimicrobials and three courses of IVIG, the child reached complete remission. In a study by Gromark et al. (2021) there was not a distinction made between PANS/PANDAS, however, the conclusions state that although full remission was rare, the majority of children with PANS significantly improved over a 3-year period post treatment.

This study also sheds light on the need for continued research related to PANDAS, such as clear definition of PANDAS remission and further research to create remission maintenance protocols. The study by Wilhelm et al. (2021) found that

achieving remission was frequent, but durable remission was rare. Regarding symptoms in remission, this study concludes of the participants, (n=84), 32 stated there are still symptom flares in remission, 9 indicated all symptoms had resolved, 18 said they have symptoms that have never resolved while in remission, and 25 parents indicated they have not yet reached remission. In a study by Leon et al. (2018), at follow-up, 29 of the 33 participants were experiencing no or only subclinical OCD symptoms. Of the remaining 4 with clinically significant OCD symptoms, one child was currently experiencing a symptom exacerbation at the time of follow-up, one child had discontinued all treatments before all symptoms had resolved, and two children had persistent OCD and remained in treatment (Leon et al., 2018). In a study by Colvin et al. (2021), the cognitive, graphomotor, and psychosocial challenges PANDAS patients face were ongoing and significant academic difficulty and emotional, behavioral, and social concerns remained after symptom resolution. This study provides a foundation for future studies to explore in more detail the concept of remission in PANDAS.

In a retrospective study of 40 patients, a study by Latimer et al. (2015) concluded that improvement with therapeutic plasma exchange was not associated with the duration of illness. In a case study by Cross et al. (2021), the researchers conclude that after a span of 31 months of illness and treatment with antimicrobials and IVIG, the patient reached complete remission. Mohammad and Dale (2018) find in PANS/PANDAS patients, there is a risk of relapse in the majority of patients. Gromark et al. (2021) concluded in PANS patients that had both chronic and non-chronic symptoms, the two groups had similar symptom severity at baseline, but the chronic course group had more impairment, which could suggest that both early onset and degree of impaired function could be useful

predictors of prognosis. Gromark et al., (2021) states that, due to their small sample size, they are not able to predict prognostic factors, but future research with larger samples should make this a priority. It is not clear if symptom flare management is life-long or if remission includes complete symptom recovery with no further exacerbations.

Implications

PANDAS Network estimates approximately 1 in 200 children suffer from PANDAS (Leonard & Swedo, 2001). This number is hard to estimate because it is believed so many children go misdiagnosed due to lack of practitioner knowledge on PANDAS. The findings of this study highlight the need for increased practitioner and community awareness of PANDAS diagnosis and treatment methods as well as future research needed to better understand PANDAS remission and treatments that could lead to lasting remission. Increasing awareness and understanding of PANDAS will lead to more children receiving timely diagnosis. Although length of illness was not found to be related to presence of remission, it is important to ensure children receive timely care in order to prevent undue lasting symptoms and family turmoil due to PANDAS. Cross et al. (2021) conducted a case study that described PANDAS symptom exacerbations as incapacitating stating that the symptoms impact the child's personal, family, social, and academic domains. Rea et al. (2021) noted that worsening school performance, increased anxiety, irritability, and aggressivity all increase with symptom exacerbations. In a study by Vlist et al. (2019) researchers sought to understand participation in childhood in those with chronic disease. Vlist et al. (2019) found that children with chronic disease learn to carefully weigh participation against their current and/or future needs and assess the risk versus benefit of their choices and chronic condition needs. Additional research for

management of the disease and potential accommodations required during PANDAS symptom exacerbations is also needed in order to help children with PANDAS thrive.

PANDAS affects the entire family, as Ringer and Roll-Pettersson (2022) discuss the negative effects PANS/PANDAS can have on parents, including the chronicity of the condition, appraisals of feeling helpless, and difficulty receiving treatment, suggests that parents of PANS/PANDAS are particularly at risk to experience high levels of psychological stress. Increasing awareness and proper diagnosis and treatment of PANDAS could lead to better mental health outcomes of the families involved, and in turn the general public.

Limitations

Limitations of this study are the parents' perceptions, whether it is mother or father completing the survey, as mothers and fathers could have different perceptions of the PANDAS experience. Another limitation could be recall bias, as parents may not clearly remember lengths of time or symptom severity. Additional limitations include conservatism, regressive bias, or consistency bias, as parents may not remember exactly how much a treatment helped or may not remember how bad or good symptoms or treatment effects were at a particular time.

A delimitation of this study is that it did not address specific brands, doses, or length of time various treatments were used, as many PANDAS patients use more than one treatment. This study found that antibiotics had the greatest healing treatment effect (n=34), but the type or dosage of antibiotic is unknown. The treatment with the next greatest healing effect was reported to be IVIG/TPE (N=16), but the type or dosage is unknown.

Another delimitation of this study is lack of clinical confirmation of diagnosis. This study did not receive medical records of participants to confirm PANDAS diagnosis from a medical professional.

Another delimitation of this study is the use of an original survey rather than an instrument that has been sufficiently tested for reliability and validity. This study used a 16-question survey on Qualtrics answered by parents of children diagnosed with PANDAS. Digital platforms for symptom tracking in PANS/PANDAS are being studied, which could lead to helpful data in understanding the relapsing/remitting course of PANDAS (Harris et al., 2021).

PANDAS remission literature is scarce, therefore there is not enough published research to employ quantitative experimental studies to determine true clinical remission factors at this time. Therefore, results of this study are limited by parental perceptions, but will serve as a basis for future research using quantitative techniques.

An assumption of this study is the understanding of the concept of remission. This word could have different meaning to different audiences related to chronic conditions. In other studies, related to remission in lupus and rheumatoid arthritis, differences in the definition of remission include remission being defined as no clinical signs of disease activity or disease activity at a low enough level that the symptoms are no longer troublesome to the patient (Wilhelm et al., 2016). Remission in PANDAS will need to be defined to address disease activity levels and if remission includes maintenance treatment. The assumption of the researcher is that remission is defined as no longer experiencing PANDAS symptoms, and does not specify remission as remission without treatment or remission while on treatment. Wilhelm et al. (2016) states that the

respondents of a study created variance in the time it takes to reach remission because of the participant's definition of remission. Therefore, having a clear definition of PANDAS remission in the future will be important in future studies.

Recommendations for Future Research

Future studies on PANDAS should be aimed at creating awareness for timely diagnosis and treatment. This study found that children were misdiagnosed or undiagnosed with PANDAS for an average length of time of 23.75 months. Although another finding of this study is that length of illness prior to receiving treatment was not found to be statistically significant in correlation to presence of remission, lack of proper diagnosis leads to unnecessary trauma and symptoms for both child and family. Rea et al. (2021) noted that worsening school performance, increased anxiety, irritability, and aggressivity all increase with symptom exacerbations. In a study by Vlist et al. (2019) researchers sought to understand participation in childhood in those with chronic disease. Vlist et al. (2019) found that children with chronic disease learn to carefully weigh participation against their current and/or future needs and assess the risk versus benefit of their choices and chronic condition needs. Future studies can be aimed at creating awareness for timely diagnosis and treatment along with investigative research to determine more specific factors in remission, such as what causes lasting symptoms or relapse and what can be done to manage and/or treat these symptoms.

Additional research needed for PANDAS should include investigative research to determine more specific factors in remission. This will include specifying PANDAS remission definitions, what causes lasting symptoms or relapse, and what can be done to manage and/or treat these symptoms. Future studies on treatments, such as how to reach

remission quickly and maintain it, are also needed, as 85% of participants in remission state they still experience PANDAS symptoms while in remission.

This study will allow for future research that can describe evidence of causation for treatment methods and factors of remission in PANDAS. This study provides several pathways for future research to continue on PANDAS treatment methods. By investigating the treatments parents reported to be most effective in remission, future studies can delve further into each area which can lead to future cause-and-effect studies to see if the phenomena occurring together provides evidence of causation. Future studies could explore which types of treatments, such as brands and dosing, have the best results for lasting remission.

Summary

The purpose of this study was to explore parents' perceptions of remission in PANDAS. Previous research could not be located that had explored factors of remission in PANDAS. This study aimed to bring hope to families suffering with PANDAS and both highlight areas needed for future research and to lead to movements to increase practitioner and community awareness of PANDAS to help more children and families reach proper diagnosis and treatment sooner without having so much time suffering. Cross et al. (2021) described PANDAS symptom exacerbations as incapacitating and affecting the child's personal, family, social, and academic domains. The aim of this study, to provide hope to families and areas for future research, has been highlighted. Jeremiah 1:5 can serve as a message for children with PANDAS, "Before I formed you in the womb I knew you, before you were born I set you apart; I appointed you as a prophet to the nations." Although the concept of remission in PANDAS requires much more

scientific research, faith remains of high importance. As the findings of this study indicate, there is hope in healing for those suffering with PANDAS, and many paths to future research that will change lives of children diagnosed with this disorder.

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APPENDIX A: SURVEY QUESTIONS

Yes/No Screening Questions:

Has your child been diagnosed with PANDAS from a medical doctor?

Are you at least 18 years of age or older?

Are you the parent of a child diagnosed with PANDAS?

What is the gender of your child? (Fill in the blank)

How old was your child at symptom onset (in years)? (Fill in the blank)

How old is your child now (in years)? (Fill in the blank)

How old was your child when they started PANDAS treatment (in years)? (Fill in the blank)

How long was the time between symptom onset and receiving official PANDAS diagnosis (in months)? (Fill in the blank)

In your opinion, which single treatment had the greatest healing effect? (Choose One: Antibiotics, Intravenous Immunoglobulin (IVIG) or Therapeutic Plasma Exchange (TPE), Tonsillectomy, Non-Prescription Supplements such as vitamins, Dietary Changes, Anti-Inflammatory Over-the-Counter drugs such as ibuprofen, prescription steroid, Other

At the height of your child's symptoms, would you classify them with mild, moderate, or severe PANDAS? Choose one: mild, moderate, severe

How long does/did a typical PANDAS flare last (in weeks)? Fill in the blank)

Has your child reached complete remission? (yes/no)

If your child has reached remission, how long did reaching remission take (in months)? Fill in the blank, N/A remission not reached

If your child has reached remission, does your child still experience symptom flares or lasting symptoms? Choose one: Yes, still has PANDAS symptoms that have never resolved, No, all PANDAS symptoms resolved, sometimes still has flares, not applicable- remission not reached

Does your child take any medications or supplements to maintain remission? Choose One: Yes, prescription medications are used to maintain remission, yes, over the counter supplements and/or lifestyle changes are used to maintain remission, no, prescription medications or supplements are not used to maintain remission, not applicable remission not reached

If your child has went through puberty, did puberty have any effect on PANDAS symptoms or remission?

Choose One: Yes puberty had an effect, less PANDAS symptoms after puberty, yes puberty had an effect, more PANDAS symptoms after puberty, puberty did not have an effect on PANDAS symptoms, not applicable- my child has not experienced puberty

APPENDIX B: SURVEY RECRUITMENT

Survey invitation to be posted on social media group pages and Aspire Newsletter, written by Janice Weddle and given to Facebook group administrators of the following pages and director of the Aspire outreach program:

Permission granted:

Facebook: PANDAS- Pediatric Autoimmune Neuropsychiatric Disorder Associated w/Strep

Administrators: [redacted]

ASPIRE PANS PANDAS Newsletter

Administrator: [redacted]

Facebook: PANDAS PARENTS

Administrator: [redacted]

Facebook: STL/Midwest PANDAS Support

Administrator: [redacted]

Permission Not Granted:

Facebook: PANDAS Resource Network

Administrators: [redacted]

No response received

Facebook: PARENTS OF CHILDREN with PANDAS/PANS/LYME/TICKBORNE DISESASES

Administators: [redacted]

Permission not granted due to study not investigating PANS

Message:

ATTENTION PANDAS PARENTS: I am conducting research as part of the requirements for a Doctor of Philosophy degree at Liberty University. The purpose of my research is to discover parents' perceptions of remission in PANDAS. To participate, you must be at least 18 years of age and the parent of a child diagnosed with PANDAS by a medical doctor, and English must be your primary language. Participants will be asked to complete a short, anonymous, online survey regarding their experience with PANDAS remission, which should take about five minutes. If you would like to participate and meet the study criteria, please follow the link below. A consent document is provided as the first page of the survey. If you agree to participate in this study, click the "proceed to survey" button at the bottom of the consent page. Thank you!

To take the survey, click here: {LINK]

APPENDIX C: ADMINISTRATOR SURVEY PERMISSION

Dear Facebook Group/Newsletter Administrator,

I am a psychology doctoral student at Liberty University, and the mom of an eleven - year-old boy diagnosed with PANDAS, located in Southern Missouri. I am requesting that you would be willing to share a survey in the [(Name of Facebook Group) Facebook Group page that you are listed as administrator on/in the ASPIRE monthly newsletter], asking for participation in my study. If you are willing to share the information, I will send information that you can simply copy and paste to potential participants that has a description of the study and link to the survey.

As part of my dissertation, I will be conducting a research project on PANDAS. The purpose of this study is to shed light on PANDAS remission experiences. As a PANDAS parent myself I understand how incredibly painstaking it is to not have answers on if or when our children will get better. I am looking for participants, parents of PANDAS diagnosed children, to complete a survey related to their experiences with remission of PANDAS. Participants who are a PANDAS parent, received PANDAS diagnosis from a medical doctor, and whose primary language is English are requested to participate.

The survey is 16 questions. The survey is not expected to take more than 5 minutes. No identifying information will be requested on the survey. I am committed to protecting privacy, and all information obtained will be kept secure with confidentiality prioritized.

There is no compensation for participating in this study, however, the benefit of being in this study is answering important questions related to PANDAS experiences that can lead to future research on effective treatment plans and can serve as a path of hope for PANDAS families. Participants are free to withdrawal or decline for any reason. Following the link on the survey that will be posted to the group pages will direct participants to a page with detailed consent information, contact information for the researcher, and more information on the purpose and procedures of the study.

Please feel free to contact me with questions or concerns, at [redacted]. You are also free to contact my dissertation chair, Dr. Laura Rolen, at [redacted]

Your assistance is very appreciated!

Please let me know if you are willing to allow this survey to be advertised on your group page. If so, I will send a follow up message with the survey link and description that can be copied and pasted onto the group page.

Sincerely,

Janice Weddle, M.Ed.

Ph.D. Candidate, Doctor of Psychology, Liberty University

APPENDIX D: CONSENT

Title of the Project: Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcal Infection (PANDAS): A Qualitative Study of Parental Perceptions of Factors in Remission

Principal Investigator: Janice Weddle, M.Ed., Ph.D. Candidate, Liberty University

Invitation to be Part of a Research Study

You are invited to participate in a research study. To participate, you must be the parent of a child diagnosed with PANDAS by a medical doctor, with English as your primary language, and at least 18 years old. Taking part in this research project is voluntary. Please take time to read this entire form and ask questions before deciding whether to take part in this research.

What is the study about and why is it being done?

The purpose of this study is to explore parents' perceptions of factors contributing to the remission of PANDAS. Research studies related to PANDAS remission and long-term outcomes are scarce and generally inconclusive. This study will look for patterns related to PANDAS remission experiences that can guide future research.

What will happen if you take part in this study?

If you agree to be in this study, I will ask you to do the following things:

This will be a 16-question online survey using Qualtrics and is only expected to take approximately five minutes to complete.

How could you or others benefit from this study?

Participants should not expect to receive a direct benefit from taking part in this study.

Benefits to society include further development on PANDAS research to both guide future research and assist parents with children with a new PANDAS diagnosis.

What risks might you experience from being in this study?

The risks involved in this study are minimal, which means they are equal to the risks you would encounter in everyday life.

How will personal information be protected?

The records of this study will be kept private. Research records will be stored securely, and only the researcher will have access to the records.

Participant responses will be anonymous.

Data will be stored on a password-locked computer with multi-factor authentication.

After three years, all electronic records will be deleted.

Is study participation voluntary?

Participation in this study is voluntary. Your decision whether or not to participate will not affect your current or future relations with Liberty University. If you decide to participate, you are free to not answer any question or withdraw at any time prior to submitting the survey without affecting those relationships.

What should you do if you decide to withdraw from the study?

If you choose to withdraw from the study, please exit the survey and close your internet browser. Your responses will not be recorded or included in the study.

Whom do you contact if you have questions or concerns about the study?

The researcher conducting this study is Janice Weddle. You may ask any questions you have now. If you have questions later, **you are encouraged** to contact her at

[redacted]. You may also contact the researcher's faculty sponsor, Dr. Laura Rolen, at [redacted]

Whom do you contact if you have questions about your rights as a research participant?

If you have any questions or concerns regarding this study and would like to talk to someone other than the researcher, **you are encouraged** to contact the Institutional Review Board, 1971 University Blvd., Green Hall Ste. 2845, Lynchburg, VA 24515 or email at irb@liberty.edu.

Disclaimer: The Institutional Review Board (IRB) is tasked with ensuring that human subjects research will be conducted in an ethical manner as defined and required by federal regulations. The topics covered and viewpoints expressed or alluded to by student and faculty researchers are those of the researchers and do not necessarily reflect the official policies or positions of Liberty University.

Your Consent

[Before agreeing to be part of the research, please be sure that you understand what the study is about. You can print a copy of the document for your records. If you have any questions about the study later, you can contact the researcher using the information provided above.

I have read and understood the above information. I have asked questions and have received answers. I consent to participate in the study.

APPENDIX E: EVIDENCE OF QUALITY

Sample Survey Responses

Female 13 16 15 36 months Antibiotics Severe 4 weeks No Not Applicable- Remission not reached Not applicable- remission not reached Not applicable- remission not reached Puberty did not have an effect on PANDAS symptoms

Female 5 7 5 0 months Anti-Inflammatory Over-the-Counter Drugs (such as ibuprofen) Severe 16 Yes Months to Remission: 6 Sometimes still has flares Yes, over-the-counter supplements and/or lifestyle changes are used to maintain remission Not applicable- my child has not experienced puberty

Male 6 13 6 one month Prescription Steroid Moderate 12 weeks Yes Months to Remission: 1 Sometimes still has flares Yes, over-the-counter supplements and/or lifestyle changes are used to maintain remission Yes puberty had an effect, more PANDAS symptoms after puberty

Female 9 13 9 3 Antibiotics Mild 4 No Months to Remission: 9 Sometimes still has flares Yes, over-the-counter

supplements and/or lifestyle changes are used to maintain remission Not applicable- my child has not experienced puberty

Female 5 11 5 1 Antibiotics Mild 8 Yes Months to Remission: 2 No, all PANDAS symptoms resolved No, prescription medications or supplements are not used to maintain remission Puberty did not have an effect on PANDAS symptoms

Female 13 25 20 84 None of these Severe 300 Yes Months to Remission: 54 Yes, still has PANDAS symptoms that have never resolved Yes, prescription medications are used to maintain remission. Yes puberty had an effect, more PANDAS symptoms after puberty

Male 4 16 6 12 Intravenous Immunoglobulin (IVIG) or Therapeutic Plasma Exchange (TPE) Moderate Several at least. Yes Months to Remission: 70 Sometimes still has flares Yes, prescription medications are used to maintain remission. Yes puberty had an effect, less PANDAS symptoms after puberty

Male 7 10 7 Within a week of onset Prescription Steroid Severe 10 Yes Months to Remission: 2-3 Yes, over-the-counter supplements and/or lifestyle changes are used to maintain remission Not applicable- my child has not experienced puberty