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PHARMACOLOGIC MANAGEMENT OF AUTISM IN TEXAS MEDICAID AND COMMERCIAL PEDIATRIC POPULATIONS

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Pharmacologic Management of Autism in Texas Medicaid and Commercial Pediatric Populations.

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Abstract

Pharmacologic Management of Autism in Texas Medicaid and Commercial Pediatric Populations.

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The objectives of this study were to 1) report the prevalence of Autism within a Texas Medicaid and rural Texas Commercial population and 2) describe the psychotropic medication utilization patterns within these populations.

Pediatric patients (<21 years) initially diagnosed with Autism between 2009 and 2012, were identified using the Texas Medicaid claims database as well as the Scott & White Health Plan claims database. Study participants had no Autism-related medical claims within 6 months before the initial Autism diagnosis. Claims were reviewed for 12 months following the initial diagnosis. After matching, pairwise comparisons were conducted to assess population differences between the two cohorts.

A total of 8,535 individuals were included in the pre-matched study population (8,260 in the Medicaid group and 275 in the Commercial group), approximately 80 percent were male in both groups.

Although the mode age was similar between the 2 groups (Medicaid = 4, Commercial = 5), the average age was lower for the Medicaid population (6 vs. 10 years $p < 0.01$). ASD prevalence in the Commercial population ranged from 0.08% in 2009 to 0.41% in 2012; and from 0.39% to 0.50% in the Medicaid population ($p<0.01$ for each year). A 2:1 match on age and gender was used to compare utilization patterns (N = 550 Medicaid; 275 Commercial). Twenty-eight percent of the overall sample population (n=231) received a prescription for at least one FDA approved anti-psychotic within the study period. The use of an approved antipsychotic was significantly greater in the Medicaid population (32%) when compared to the rural Commercial population (23%; $p< 0.01$). Specifically, risperidone utilization was greater in the Medicaid population (22%) when compared to the Commercial population (15%; $p<0.01$). The use of non-FDA approved antipsychotic medications was also significantly greater in the Medicaid population (13%) compared to Commercial patients (9%; $p=0.01$).

Based on the results of this study, over one-fourth of the Autistic population was being treated with medications that have been FDA approved for the treatment of Autism. However, despite limited evidence related to long term safety and efficacy, several off-label psychotropic medications continue to be used in this population.

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Chapter 1: Literature Review

Introduction

The origin of Autism, as it is understood today, can be traced back to a 1943 article published by Leo Kanner, the 20th century father of child psychiatry. In the landmark case series, Kanner examined 8 boys and 3 girls under the age of 11, referred to him by their parents for psychiatric evaluation.[1] He concluded that, a unique syndrome of "extreme autistic aloneness" was the underlying pathology responsible for the children's atypical behavior. The syndrome was characterized by profound autistic withdrawal, challenging behavior, an insistence on sameness, a limitation in variety of spontaneous activity, language deficits, and a preoccupation with objects rather than people.[1] Kanner also noted that the children were born to intelligent and prominent families, with a history of psychiatric illness.[1]

Not long after the publication of Kanner's article, Bruno Bettelheim, an emerging leader in the field of psychology, began circulating the idea that Autism is not a neurodevelopmental disorder but rather a result of emotional detachment.[2,3] Bettelheim postulated that children are not born with Autistic predisposition, but rather influenced into the condition by "refrigerator parents".[2] The lack of emotional display on the part of parents results in the manifestation of Autistic signs in children, as well as a general disinterest in human interaction. Bettelheim argued that if Autistic children are separated from the cold, unemotional environments of their homes, they can be fully 'cured'.[2] This theory persisted for several decades. As a result, several psychoanalytic treatment methods were developed.[2,3]

By the early 1970s, the anti-psychiatry movement had fully emerged; along with the idea that psychogenic modes of treatment may do more harm than good. Advancements in neurobiology provided a better understanding of the genetic origin of psychiatric illness and

made it easier to suggest a neurologic basis for the development of Autism. The results of Bettelheim's experiments could not be replicated by researchers using similar methodologies and significant doubt was cast on his research conclusions.[2] Despite the controversy surrounding the work of Bettelheim, the exploration of psychoanalysis as a potential treatment option in Autism made it clear that psychoanalytic interventions are useful in modifying the behavior of Autistic children.[2] This understanding soon gave rise to the Applied Behavior Analysis (ABA) treatment model. To date, ABA is successfully employed by many clinicians to create a framework of learning for Autistic children.[3,4]

Much like its history, the present understanding of Autism and its origin remain controversial. Advancements in genetic mapping and neuroimaging technology have allowed scientists to identify particular areas of 'enhancement' in the Autistic brain: increased white matter, gray matter, and cerebellar white matter volumes.[5] However, Autism remains a multifaceted neuropsychiatric disorder with highly variable manifestations. Diagnosing Autism requires the use of a combination of objective and subjective measurements by an experienced clinician.[3,6]

Epidemiology

The complexity of the Autism diagnosis is reflected in the multiple revisions to its diagnostic criteria since 1980 when it was initially recognized by the American Psychiatric Association. The fourth edition text revision of the Diagnostic and Statistical Manual (DSM-IV TR), published in 2000, identifies a triad of symptoms in the diagnostic criteria for autistic disorder: 1) qualitative impairment is social interaction, 2) qualitative impairments in communication, and 3) restricted, repetitive and stereotyped patterns of behavior, interests, and activities.[3,6] Individuals should display delayed or abnormal functioning in social interaction, social language, communication, or symbolic or imaginative play prior to age 3.[3,6] Finally,

disturbances in development may not be better accounted for by Rett's Disorder or Childhood Disintegrative Disorder.[3,6]

DSM-IV TR distinguishes the diagnosis of Autism from Pervasive Developmental Disorder not otherwise specified and Asperger's Disorder, conditions commonly associated with Autism. Pervasive Developmental Disorder, otherwise referred to as Atypical Autism, is vaguely defined in DSM-IV TR as severe social impairment not meeting criteria for any other Pervasive Developmental Disorder (such as Asperger's Disorder, Rett's Disorder and Childhood Disintegrative Disorder).[6] According to DSM-IV, this diagnosis is meant to include individuals presenting with Autistic symptoms after 36 months or those with subthreshold manifestations of Autism.[6] DSM-IV also identifies Asperger's Disorder as a unique clinical syndrome distinguishable from Autism in that those with Asperger's exhibit no clinically significant delays in language or cognition.[6] With these definitions in mind, it may be difficult to distinguish high functioning Autism from Asperger's Disorder.

The newest edition of the Diagnostic and Statistical Manual (DSM-V), attempts to incorporate these three very similar diagnoses into one all-encompassing clinical condition. Published in 2013, the DSM-V excludes the diagnoses of Asperger's Disorder, and Pervasive Developmental Disorder not otherwise specified.[3] These conditions have been incorporated into the broadened diagnosis of Autism Spectrum Disorder (ASD) by eliminating the requirement for speech delay and expanding the stereotypic behavior criterion to include hyper- or hyporeactivity to sensory stimuli. Table 1.1 compares the diagnostic criteria and highlights the differences between DSV-IV and DSM-V.[3]

Table 1.1: Comparison of diagnostic categories for autism-related disorders in DSM-IV and DSM-V.

DSM-V Neurodevelopmental disorders	DSM-IV-TR Pervasive developmental disorders
A09: Autism spectrum disorder (includes specification of severity of symptoms)	299.00: Autistic disorder
Excluded	299.80: Rett's disorder
A09: Autism spectrum disorder (does not include reference to prior development)	299.10: Childhood disintegrative disorder
A09: Autism spectrum disorder (includes specification of severity of symptoms)	299.80: Asperger's disorder
A09: Autism spectrum disorder (includes specification of severity of symptoms)	299.80: Pervasive developmental disorder not otherwise specified (including atypical autism)

Source: Durand, M. (2014). Autism Spectrum Disorder: A clinical guide for general practitioners. Washington, DC: American Psychological Association.

Note: DSM-5= Diagnostic and Statistical Manual of Mental Disorders 5th edition; DSM-IV-TR=Diagnostic and Statistical Manual of Mental Disorders 4th edition text revision.

Though individuals may present at any end of the Autistic spectrum, numerous studies have sought to describe the Autistic population.[7-13] In 2014, the reported prevalence of Autism in the pediatric population was close to 1.5%.[14] This is a marked increase from a reported prevalence of 0.3% in 2008.[3] Some attribute this increased prevalence to broader applications of the diagnostic criteria in order to ensure access to social services. Others suggest that environmental influences may play a role.[2,7,8,10] Despite the controversy regarding its origin, the central role of genetics in Autism has been well established. Individuals with an Autistic sibling are 20-50 times more likely to develop Autism when compared to the general population.[11] In addition, advanced maternal and paternal age has been associated with an increased risk of Autism.[9,10]

Clinical signs of Autism typically manifest before 36 months of age; this early presentation is included in the condition's diagnostic criteria.[4,6] However, mild variations have been observed in individual populations. The age at diagnosis has been shown to be greater in low income communities when compared to high income communities.[12,13] Variances in Autism prevalence have also been documented. The prevalence of Autism has also been shown to be lower in non-Hispanic black and Hispanic populations when compared to non-Hispanic white and Asian populations.[12] It may be argued that this observed difference is a result of under-diagnosis rather than an inherent difference between the populations. When populations are adjusted for income, this difference in prevalence is no longer observed.[12] The incidence of Autism also appears to differ by gender. Compared to females, males are up to four times more likely to receive an Autism diagnosis.[3,13]

Burden of Illness

Receiving an ASD diagnosis is often a distressing family experience. Family members report a multitude of emotions including fear, guilt, shock, resentment and possibly relief at the validation of an ASD diagnosis.[3,4] After identifying a child's condition, families are frequently faced with the burden of navigating a complex health system to obtain needed healthcare resources.

Since the ASD diagnosis is often made in early childhood, parents and siblings play a key role in family adaptation. The emotional burden on families may correlate directly with a child's symptom severity and number of comorbidities.[3,4] As a result, the variability in cognitive impairment across the Autism spectrum and the ambiguity of each child's prognosis may be additional sources of stress to parents of Autistic children. Parents may have difficulty maintaining occupational responsibilities and self-care due to the all-encompassing nature of their child's illness. Younger siblings of children with Autism report feelings of loneliness and

neglect as well as resentment related to problem behaviors in the Autistic child.[3,4] Elder siblings of Autistic children appear to be positively affected and report increased levels of self-efficacy and social competence.[3,4]

Children with Autism are greater utilizers of healthcare resources when compared to their non-autistic counterparts.[15,16] Many children with Autism suffer from multiple comorbidities including depression, anxiety, gastrointestinal distress, insomnia, hypersomnia and seizure disorders.[11] The seizure risk in the Autistic population is 20 to 30 times higher than that in the general population; those with a seizure co-morbidity often require more frequent outpatient visits and in some cases hospitalization.[3] The most commonly occurring co-morbidity, intellectual disability, is predictive of poor long-term outcomes.[11]

The cost of caring for an Autistic child may be initially perceived as a parent's responsibility but a more in depth review of U.S. legislation reveals that a majority of these costs are absorbed at the state level. Up to thirty-eight percent of Autistic children present with a comorbid diagnosis of intellectual disability.[3,8,15] The Individuals with Disabilities Education Act (IDEA) of 1997 mandates the provision of special education services to all children, 3 to 21 years of age, with a diagnosed disability. IDEA not only requires the provision of disability services, but stipulates that the services provided must apply research proven methods of teaching and learning. In other words, states are not only required to provide disability services to children, they are also called upon to document the effectiveness of these special education programs. The provision of effective, evidence-based special education services comes at a significant cost. A 2007 article on special education expenditures estimated that the state of Texas spends approximately $11,000 dollars annually per child enrolled in special education.[4] However, without timely and appropriate intervention, it is estimated that an individual with

ASD may cost the U.S. up to 3.2 million dollars over the course of his or her lifetime.[4] Despite the implicit cost savings associated with the provision of special education services, these services may cause significant strain on already tight state budgets. Medicaid costs in providing care to children with ASD rose by over 32 percent between 2000 and 2003; those with intellectual disability cost the program 50% more than those without.[2,4]

With rising costs in mind, it is understandable that over 30 percent of states have passed legislation mandating private insurers to cover behavioral interventions in Autism treatment.[4] While this strategy of cost deferment may temporarily offset strain on the state budget, it lacks long term sustainability. Increased healthcare expenditures on the part of insurers eventually results in increased member premiums as insurers attempt to maintain financial viability. In essence, the cost burden is shifted from organizations to individuals. Since the costs associated with caring for children with ASD can't be eliminated, only shifted, it becomes imperative to ensure that the dollars allocated for the treatment of Autism Spectrum Disorders are being used in a timely manner, on treatment methods that have proven to be effective.

Non-Pharmacologic Treatment Options

No single intervention can be applied unilaterally to treat all ASD symptoms. Rather, individual deficits are identified through assessment of the core areas of dysfunction: social, communicative, and behavioral. Interventions are then tailored to target particular deficit areas. Interventions for the treatment of core symptoms of ASD are largely educational. To date, no medical interventions have demonstrated improvement in core symptoms of ASD. Medical interventions are applied as a form of palliation to address ASD's associated symptoms (i.e., seizure, problem behaviors, etc.).

The comprehensive behavioral treatment programs with empiric support can be divided into 2 major categories: 1) behavioral programs using applied behavior analysis techniques, 2) behavioral programs integrating developmental consideration to guide treatment targets.[4] The effectiveness of interventions increases when they are begun between ages 2 and 4 and administered with intense frequency (at least 25 hours per week for at least 2 years).[2-4,6]

Applied Behavior Analysis

Applied Behavior Analysis (ABA) is the only recognized, safe and effective treatment for Autism. First used in the Autistic population in the 1960s, it is useful in teaching simple (i.e., maintaining eye contact) as well as complex tasks (i.e., empathy).[4,17] The goal of treatment is to increase useful behaviors through coaching and positive re-enforcement while decreasing harmful or undesirable behaviors.[4,17]

ABA may take various forms and is most appropriately viewed as a teaching style that encompasses various types of interventions rather one particular intervention. Treatments and interventions can be provided individually or in a group setting. Effective programs are customized to meet the learner's needs.[4,17]

Studies show ABA is beneficial in all age groups from pre-school to adult aged individuals.[4,17] Participation in an ABA program has been shown to improve social interactions and increase involvement in family and community activities.[17] Across studies, a small proportion of children respond minimally to ABA.[17] Currently, there is no scientific method useful in predicting response to treatment.

ABA techniques vary in complexity and duration. "Early Intervention" programs begin before age 5 while "intensive' programs are administered for 25 to 40 hours each week for 1 to 3 years.[4] Studies have examined the benefit of combining multiple techniques to treat several skill deficits.[4] Despite the variation in individual programs, effective treatments should incorporate proper planning and progress assessment, and be provided by a trained specialist.[17]

Developmental Treatment Approaches

Developmental interventions apply the principles of developmental science and use typical child development sequences as a framework for planning and evaluating treatment programs. Developmental interventions are often used in conjunction with behavioral interventions such as ABA.[17]

The Developmental Individual Differences, Relationship-Based Floortime Model is an approach most commonly used in infants, toddlers and preschoolers. The primary goal of this treatment approach is to facilitate the child's view of himself/herself as an intentional, relational being and to build, cognitive, language and social capabilities.[4] Therapists, educators and parents participate in 'floor-time' exercises: unstructured play sessions in which the adult follows the child's lead in interactions with his or her environment. Ultimately this approach seeks to build trusting relationships that encourage shared attention, interaction and communication.

The Denver Model and Early Start Denver Model is utilized in children as young as 12 months up to 5 years. This interdisciplinary approach has a focus on social communication.[4] Parents are often involved in administering interventions which are child-centered and play based.

Other Developmental treatment models include: Hanen's More than Words; Joint Attention Mediated Learning; Relationship Development Intervention; Emotional Regulation,

and Transactional Support; and Treatment and Education of Autistic and Related Communication Handicapped Children.[4]

Overarching themes in these models are the need for parental involvement in program development, the absence of high quality evidence in support of these interventions, child centeredness, an emphasis on early intervention (beginning as early as 12 months), and a need for consistent one on one instruction with parents or educators (on average, over 20 hours per week).

Controversial Treatments

The Task Force on Promotion and Dissemination of Psychological Procedures defines a well-established treatment as one with a minimum of two studies indicating treatment is superior to an established treatment or placebo.[4] Studies must be conducted by at least 2 independent researchers.

The gluten and casein-free diet, a reported Autism treatment, was developed based on the opioid excess theory.[4] When hydrolyzed into individual proteins, gluten and casein cross the blood brain barrier and attach to the opioid receptor. The opioid excess theory asserts that opioid over activity results in the manifestation of ASD symptoms including panic attacks, self-mutilation, hyperactivity, and constipation.[4] Individual case reports have demonstrated treatment benefits, however these benefits are yet to be replicated in large, randomized controlled trials.[4] Parents and caregivers should be aware of the adverse effects of treatment which include decreased bone mineral density and protein malnutrition.

Other non-pharmacologic treatments include hyperbaric oxygen treatment, chelation therapy, animal therapy, sensory and auditory integration therapies, and facilitated communication.[4] A principal theme evident in the evaluation of these treatment strategies is a

lack of high quality evidence supporting their efficacy and the potential for adverse treatment effects associated with their use.

Pharmacologic Treatment Options

Before conducting a review of the pharmacologic options available for the treatment of Autism Spectrum Disorders, it is important to clarify that none of these agents have demonstrated efficacy in managing the core symptoms of ASD. Pharmacologic interventions serve only as a form of palliation and may be useful in treating comorbid conditions associated with ASD.

Prescription Treatment Options

Various studies have sought to describe the use of prescription medications within the Autistic population.[15,16,18-28] A majority of studies report that psychotropic medications are the most commonly used class of drugs in this population with reported prevalence rates ranging from 30 to 70 percent.[16,18,19,21-24,26] This trend is consistent internationally and has been replicated in countries such as the United Kingdom and Japan.[22] However, when compared to other nations, the U.S. population has a greater prevalence of psychotropic medication use.[22] Prescription patterns vary by physician specialty with stimulant medications being more commonly prescribed by pediatricians and antipsychotics more commonly prescribed by psychiatrists.[26]

The use of psychotropic medications appears to increase over time for all major psychotropic classes.[16,26] The likelihood of being on one or more psychotropic medications increases with age, Medicaid eligibility, and Caucasian ethnicity.[12,16,19,26] A 2008 study of the U.S. Medicaid population revealed that children with a diagnosis of Asperger's disorder or pervasive developmental disorder not otherwise specified are approximately 10% more likely to be prescribed psychotropic drugs than children with a diagnosis of autistic disorder.[26] Autistic individuals with one or more comorbid psychiatric diagnoses also have higher rates of

psychotropic medication use with rates highest among individuals with schizophrenia or bipolar disorder.[18]

Antipsychotics

Antipsychotics are the mostly commonly prescribed class of psychotropic medications in individuals with ASD, with reported prevalence rates as high as 40 percent.[18,19] This class of drugs includes the only FDA approved medications indicated for the treatment of Autism's associated symptoms. Parents of children with Autism have reported partial benefits with the use of antipsychotics.[3] Risperidone is the most commonly prescribed agent in this class, with prevalence rates as high as 19%, followed closely by aripiprazole (11%).[18,19]

Risperidone was initially approved for use by the FDA in 1993 and did not receive its indication for the treatment of irritability and aggression associated with autistic disorder in patients 5 years and older until 2006.[29] Three short-term, placebo-controlled clinical trials in Autistic children and adolescents aged 5 to 17 years demonstrated clinical improvement in irritability, social withdrawal, and hyperactivity measured using the irritability subscale of the Aberrant Behavior Checklist.[29] Results also showed modest improvements in stereotypy and inappropriate speech when compared to placebo.[29] Following the initial short-term studies, the long-term effectiveness of risperidone was demonstrated in a 4 to 6 month open-label study extension.[29]

An atypical antipsychotic, risperidone acts a mixed serotonin-dopamine antagonist by binding to ($5HT_2$) and, with lesser affinity, dopamine receptors (D2R) in the central nervous system.[29] The deceased comparative affinity of this agent for the dopamine- receptor (D2R) is thought to reduce negative symptoms of psychosis or self-injury while also reducing the incidence of extrapyramidal side effects.

Aripiprazole was approved for use by the FDA in 2002; it received its indication in Autism in 2009.[30] Among its many indications, this agent is approved for the treatment of irritability associated with Autistic disorder in children 6 years of age and older. Two randomized, controlled clinical trials in Autistic children age 6 to 17 years of age demonstrated significant clinical improvement in irritability, measured using the irritability subscale of the Aberrant Behavior Checklist, when compared to placebo.[30] Like risperidone, aripiprazole is an atypical antipsychotic and exerts its effects by binding to several dopamine and serotonin receptors. It also has a moderate affinity for $alpha_1$-adrenergic receptors as well as histamine-1 receptors.[30] Other, non-FDA approved, antipsychotics reported in the literature include olanzapine, quetiapine, ziprasidone, haloperidol, and chlorpromazine.[18,19]

Other psychotropic medications

The use of other psychotropic medications in the management of Autistic symptoms has been well established in the literature. [15,16,18-28] Stimulants appear to be the second most commonly used class of medications, followed by anti-depressants. [18,19] The use of mood stabilizers, sedatives, anti-hypertensives and anticonvulsants has also been reported in the literature.[18,19] Table 1.2 lists these different medication classes including the prevalence of their use in treating ASD associated symptoms, and documented indications.[5,18-19,21]

Table 1.2: Medication classes used in the treatment of ASD associated symptoms, their prevalence, and indications for use.

Medication Class	Reported Prevalence	ASD Symptoms (Indications)
Antipsychotics	12-45%	Aggressive behavior, self-injurious behavior, ritualistic behaviors
Stimulants	6-20%	Tics, impulsivity, hyperactivity,
Anti-depressants	6-21%	Anxiety, depression, ritualistic behaviors
Mood Stabilizers	4%	---
Sedatives	3-9%	Insomnia
Anti-hypertensives	5-13%	Tics, hyperactivity
Anticonvulsants	11-18%	Seizures, epilepsy

Sources: Levy SE, Mandell DS, Schultz RT. Autism. Lancet. 2009 Nov 7;374(9701):1627-38. doi: 10.1016/S0140-6736(09)61376-3. Epub 2009 Oct 12. Review. Erratum in: Lancet. 2011 Oct 29;378(9802):1546. Aman MG, Lam KS, Collier-Crespin A. Prevalence and patterns of use of psychoactive medicines among individuals with autism in the Autism Society of Ohio. J Autism Dev Disord. 2003 Oct;33(5):527-34. Aman MG, Lam KS, Van Bourgondien ME. Medication patterns in patients with autism: temporal, regional, and demographic influences. J Child Adolesc Psychopharmacol. 2005 Feb;15(1):116-26. Baribeau DA, Anagnostou E. An update on medication management of behavioral disorders in autism. Curr Psychiatry Rep. 2014 Mar;16(3):437.

Non-prescription treatment options

Researchers have documented that over 30% of the ASD population is being treated with complementary and alternative medications including dietary supplements and vitamins.[4] On average, parents concurrently use as many as 7 different treatments per child.[4] Not only does polypharmacy present a problem from a safety perspective, the use of multiple medications concurrently may also confound the benefits of truly effective agents. This confounding effect is of particular concern in the Autistic population considering the shortage of literature supporting the effectiveness of complementary and alternative treatments.

Complementary and alternative medication classes are often use in conjunction with or as a replacement of conventional treatment strategies. A 2011 review of the literature on complementary and alternative medication (CAM) use in the Autistic population reveals that dietary supplements are the most commonly used CAM.[23] The use of supplements appears to increase with parental education and decrease as patients age. [4,23,28]

The use of micronutrients, such as vitamins, has also been reported in the literature. In a 2010 retrospective, case-control study, micronutrient management resulted in lower activity level, less social withdrawal, less anger, better spontaneity in relation to the examiner, less irritability, lower intensity of self-injurious behavior, markedly fewer adverse events and less weight gain when compared to prescription medications.[28] However, the results of this study are yet to be replicated in a randomized, controlled trial.

Monitoring/Adverse Effects

When discussing the use of medications in the Autistic population, the need for appropriate follow-up and monitoring for adverse effects should not be overlooked. Metabolic changes associated with the use of atypical antipsychotic medications have been well documented.[29,30] No differences have been observed in the incidence of metabolic changes when comparing aripiprazole to risperidone.[29,30] However, weight gain associated with risperidone or aripiprazole use appears to be dose responsive.[30] When using antipsychotics, children may also be at risk of developing extra-pyramidal symptoms, dyskinesia, and prolactin-related adverse effects.[29,30]

Children receiving antipsychotics for the treatment of Autism related symptoms should be evaluated at baseline, 3 months, 6 months and every 6 to 12 months thereafter.[20,27] Baseline measures should include: 1) baseline ECG; 2) complete family history with an emphasis on cardio-metabolic illness; 3) blood work (including fasting lipid profile, glucose, hemoglobin A1C, prolactin level, liver enzymes); 4) weight, blood pressure, abdominal circumference; 5) documentation regarding presence of extrapyramidal symptoms. Follow-up evaluations should incorporate items 3-5 above as well as an assessment of treatment response.[27]

The use of other classes of medications for the treatment of other associated symptoms, such as attention deficit hyperactive disorder, should follow the monitoring recommendations of their respective medical associations.[4]

Study Objectives

Approximately 400,000 infants are born in the state of Texas each year – the second highest number in the nation.[14] Studies have shown that the use of antipsychotics and other psychotropic medications within the Autistic population increases with age and that low income children or children on Medicaid are more likely to receive these medications. [12,16,19,26] It has also been reported that there is a significant amount of off-label and investigational drug use within this population. [15,16,18-28] As the number of Texas children with Autism grows, it is becoming increasingly important to develop an understanding of the demographics of the Texas Autistic population, as well as their pharmacologic management and medication utilization patterns. Specific objectives and hypotheses of this study include:

1. To report the prevalence of diagnosed Autistic Spectrum Disorders (ASDs) in the Texas Medicaid and Commercial populations within the study period.

    H_o1.1: When compared to a rural Commercial population, there is no statistically significant difference in the prevalence of ASD diagnoses in the Texas Medicaid population.

2. To report the average age, at time of diagnosis, of individuals with an ASD diagnosis in the Texas Medicaid and Commercial populations.

    Ho2.1: When compared to a rural Commercial population, there is no statistically significant difference in the average age of individuals with an ASD diagnosis in the Texas Medicaid population.

3. To describe the patterns of psychotropic medication use in the Texas Medicaid and Commercial populations diagnosed with ASD.

    H_o3.1: When compared to a rural Commercial population, there is no statistically significant difference in the prevalence of use of one or more FDA approved antipsychotic medications within the Texas Medicaid population.

    H_o3.2: When compared to a rural Commercial population, there is no statistically significant difference in the prevalence of use of one or more non- FDA approved antipsychotic medications within the Texas Medicaid population.

    H_o3.3: When compared to a rural Commercial population, there is no statistically significant difference in the prevalence of use of aripiprazole within the Texas Medicaid population.

    H_o3.4: When compared to a rural Commercial population, there is no statistically significant difference in the prevalence of use of risperidone within the Texas Medicaid population.

    H_o3.5: When compared to a rural Commercial population, there is no statistically significant difference in the prevalence of use of any psychotropic medication within the Texas Medicaid population.

H_o3.6: When compared to a rural Commercial population, there is no statistically significant difference in the average number of unique psychotropic medications prescribed within the Texas Medicaid population during the study period.

H_o3.7: Among patients being treated with a psychotropic agent, when compared to a rural Commercial population, there is no statistically significant difference in the proportion of individuals being followed by a psychiatrist, neurologist, or developmental pediatrician within the Texas Medicaid population.

Chapter 2: Methodology

Study Design and Data Source

This study was a retrospective, descriptive study. A longitudinal review of existing medical and pharmacy claims data was be conducted. Data specific to the Medicaid population was obtained from the Texas Medicaid Vendor Drug Program. In March 2015, over 4 million children were insured through Texas Medicaid, the third largest state Medicaid program in the nation.[31] Commercial claims data was obtained from Scott & White Health Plan (SWHP), a regional health plan located in central Texas. As part of an integrated health system, SWHP provides access to medical claims, pharmacy claims, as well as electronic medical records. Currently, the plan insures close to 125,000 Commercial lives. This study was approved by the Scott & White Health System and University of Texas at Austin institutional review boards (IRBs) following expedited review.

Study Sample

Members, 0 to 21 years of age, with one Autism related inpatient or outpatient ICD-9 (299, 299.00, or 299.80) between January 1st, 2009 and December 31st, 2012 were eligible for study inclusion. Participants were required to have a minimum of 18 months continuous enrollment within the study period. The date of the first Autism related ICD-9 was defined as the subject index date. Members were followed for 12 months post index to identify differences between study populations. Study participants with an Autism related ICD-9 within 6 months prior to the index date were excluded from analysis (objectives 2 and 3).

Study Variables

The following data parameters were collected on medical and pharmacy claims: member ID, member date of birth, member gender, provider National Provider Index (NPI), date of prescription drug fill, drug name, drug American Hospital Formulary System (AHFS) code, medical claim date, primary claim diagnosis, and other diagnoses associated with each medical claim.

Calculations related to the prevalence of Autism Spectrum Disorders were conducted using the following ICD-9s: 299 (Pervasive Developmental Disorder), 299.80 (Asperger's Disorder), and 299.00 (Autism). FDA approved antipsychotics included all strengths and dosage forms of risperidone and aripiprazole. Non-FDA approved antipsychotics were defined as all strengths and dosage forms of all medications, excluding risperidone and aripiprazole, with an American Hospital Formulary System (AHFS) code of 281608. 'Psychotropic' medications were defined as all medications in the following therapeutic classes: antipsychotics, antidepressants, stimulants, mood stabilizers, benzodiazepines, and anticonvulsants. Physician specialty was determined using the Baylor Scott & White Health System Provider Index.

Statistical Analyses

Demographic variables including gender, and age (at index) were summarized using descriptive statistics. Categorical variables such as prevalence of ASD diagnosis, and prevalence of medication use were reported using frequencies and proportions. Continuous variables such as age were reported using means and standard deviations. Count variables such as the number of psychotropic medications prescribed were summarized using means and standard deviations.

Pairwise comparisons were conducted to detect population differences in discrete as well as continuous variables. Independent sample t-tests and ANOVA were used to detect differences

in means for continuous and discrete variables. Chi-squared analyses were used to detect differences in categorical variables.

Study participants were matched on age, and gender. Statistical tests for each variable are provided in Table 2.1. Analyses were conducted using SAS 9.4. An a priori alpha level of 0.05 was set for all statistical analyses.

Table 2.1: Statistical tests used for pairwise comparisons between the Commercial and Texas Medicaid populations.

Variable Name	Variable Type	Statistical Test	Objective(s)
ASD diagnosis prevalence	Categorical	Chi-Squared	H_o1.1
Medication use prevalence	Categorical	Chi-Squared	H_o3.1-H_o3.5
Proportion followed by specialist	Categorical	Chi-Squared	H_o3.7
Gender	Categorical	Chi-Squared	---
Age	Continuous	Independent sample t-test	H_o2.1
Number of psychotropic medications prescribed	Discrete (Count)	Kruskal Wallis test	H_o3.6

Chapter 3: Results

Study Sample

A total of 27,608 Texas Medicaid and 422 Commercial members with a medical claim of 299.80, 299.00, or 299 were identified during the study period. Commercial members included in this study were not insured by Texas Medicaid during the study period. After applying study inclusion criteria, the study population included a total of 8,535 individuals, 275 within the Commercial population and 8, 260 in the Texas Medicaid population. Table 3.1 reports the sample size after applying each inclusion criterion.

Table 3.1 Member Selection

Selection Criteria	Sample Size (N)	
	Medicaid	**Commercial**
At least one medical claim for Autism[a] between 01/01/2009	27,608	422
to 12/31/2012	(100.0%)	(100.0%)
18 months continuous enrollment within study period	23,561	377
	(85.3%)	(89.3%)
12 months continuous enrollment post-index and no medical	8,261	275
claim for Autism[a] within 6 months pre-index	(29.9%)	(65.2%)
No missing demographic information (age, gender)	8,260	275
	(29.9%)	(65.2%)

[a]*ICD-9: 299.00, 299.80 or 299*

Of the 8,535 individuals included in the final study population, approximately 80 percent were male. No difference in gender was observed between the two populations (p=0.27). The distribution of age in the overall population was left skewed, therefore medians were reported, in addition to sample means, as an appropriate measure of central tendency. The median age at

index of the overall population (n=8,535) was 6 years old. The results of an independent sample T-test revealed that, on average, members of the Medicaid population were 3 years younger than those in the Commercial population when first diagnosed (p<0.001).

Table 3.2 Population Demographics

Gender	**Commercial**	**Medicaid**	**Overall**	**P-value**
Female (N,%)	55 (20%)	1882 (23%)	1937 (23%)	=0.2781
Male (N,%)	220 (80%)	6378 (77%)	6598 (77%)	

Population (N)	**Mean Age (S.D.)**	**Median**	**Mode**	**Minimum**	**Maximum**	**P-Value**
Medicaid (8,261)	7.39 (4.64)	6	4	0	20	<0.0001
Commercial (275)	9.93 (4.30)	10	5	1	20	
Total (8,535)	7.47 (4.65)	6	4	0	20	---

Prevalence of Autism Diagnosis

The prevalence of the Autism diagnosis was examined in both populations prior to the application of inclusion criteria. Prevalence was calculated each year within the study period. A positive trend was observed as prevalence increased in both populations with each successive year. ASD prevalence in the Commercial population ranged from 0.08% in 2009 to 0.41% in 2012. In the Medicaid population, ASD prevalence ranged from 0.39% to 0.50% from the beginning to the end of the study period. The observed prevalence was significantly greater in the Medicaid population each year ($p<0.0005$).

Table 3.3 Prevalence of Autism Diagnosis in Commercial and Medicaid Populations (2009-2012)

Year[a]	Commercial (N, %)	Medicaid (N, %)	P-Value
2009	132 (0.08%)	10,646 (0.39%)	<0.0001
2010	375 (0.33%)	13,499 (0.45%)	<0.0001
2011	391 (0.35%)	16,537 (0.51%)	<0.0001
2012	343 (0.41%)	16,442 (0.50%)	<0.0003

[a] *Commercial year= calendar year; Medicaid year=Texas Medicaid fiscal year*

Psychotropic medication use patterns

Several chi-squared analyses were conducted to detect differences in the psychotropic medication use patterns of the Medicaid population compared to those of the Commercial population. Prior to conducting these analyses, study participants were matched 2:1 on age and gender. The resulting sample included 275 members of the Commercial population and 550 members of the Medicaid population. Eighty percent of the final population was male, with an average age of 9.99 (S.D. 4.41) and median age of 10.

Two hundred and eighty-three unique medications were prescribed to the matched study population within the follow-up period. Appendix A lists the medication names included in each treatment class. Within the overall matched sample population (n = 275 Commercial: n= 550 Medicaid; Total n=825), stimulants were the most commonly used psychotropic medication class (52%) followed by FDA approved antipsychotics: risperidone and Aripiprazole (28%), and anti-depressants (26%). The same pattern of use was observed in the Medicaid population. See Table 3.4

Stimulants were the most commonly prescribed psychotropic medication class within the Commercial population (80%). However, within the Commercial population, the use of antidepressants (48%) was more common than that of FDA approved antipsychotics risperidone and Aripiprazole (23%).See Table 3.4.

Among the female population (n=165), stimulants were again the most commonly prescribed psychotropic medication class (47%), followed by antidepressants (34%) and FDA approved antipsychotics (29%). The same pattern of use was observed in the Commercial population. However, within the Medicaid population, stimulants were most commonly used

(37%) followed by FDA approved antipsychotics (34%) and anticonvulsants (27%). See Table 3.5

Among the male population (n=660), stimulants were the most commonly prescribed psychotropic medication class (57%) followed by FDA approved antipsychotics (28%) then antidepressants (25%). The same pattern of use was observed in the Medicaid population. However, within the Commercial population, the prevalence of use of stimulants (65%) was followed by antidepressants (35%) then FDA approved antipsychotics (21%). See Table 3.6.

Table 3.4 Proportion of Sample Population with One or More Prescriptions in each Medication Class

Total Population (N=825)

Medication Class	**Medicaid (N, %)**	**Commercial (N, %)**	**Total (N, %)**
FDA Approved:			
Risperidone	122 (22%)	40 (15%)	162 (20%)
Aripiprazole	53 (10%)	17 (8%)	70 (8%)
Non-FDA Approved Antipsychotic	70 (13%)	20 (9%)	90 (10%)
Anti-depressant	117 (21%)	107 (48%)	224 (26%)
Stimulant	271 (49%)	180 (80%)	451 (52%)
Mood Stabilizer	58 (11%)	8 (4%)	66 (8%)
Benzodiazepine	72 (13%)	13 (6%)	85 (10%)
Anticonvulsant	95 (17%)	16 (7%)	111 (13%)
Other Psychotropic Agent	27 (5%)	23 (10%)	50 (6%)
Other Non-psychotropic Agent	47 (9%)	266 (96%)	313 (36%)

Table 3.5 Proportion of Females in Sample Population with One or More Prescriptions in each Medication Class

Female Population (N=165)

Medication Class	Medicaid (N, %)	Commercial (N, %)	Total (N, %)
FDA approved			
Risperidone	25 (23%)	7 (13%)	32 (19%)
Aripiprazole	12 (11%)	4 (7%)	16 (10%)
Non-FDA Approved Antipsychotic	14 (13%)	5 (10%)	19 (12%)
Anti-depressant	26 (24%)	30 (55%)	56 (34%)
Stimulant	41 (37%)	36 (65%)	77 (47%)
Mood Stabilizer	8 (7%)	2 (4%)	10 (6%)
Benzodiazepine	26 (24%)	5 (9%)	31 (19%)
Anticonvulsant	30 (27%)	2 (4%)	32 (19%)
Other Psychotropic Agent	6 (5%)	3 (5%)	9 (5%)
Other Non-psychotropic Agent	9 (8%)	55 (100%)	64 (39%)

Table 3.6 Proportion of Males in Sample Population with One or More Prescriptions in each Medication Class

Male Population (N=660)

Medication Class	Medicaid (N, %)	Commercial (N, %)	Total (N, %)
FDA Approved			
Risperidone	97 (22%)	33 (15%)	130 (20%)
Aripiprazole	41 (9%)	13 (6%)	54 (8%)
Non-FDA Approved Antipsychotic	56 (13%)	15 (7%)	71 (11%)
Anti-depressant	91 (21%)	77 (35%)	168 (25%)
Stimulant	230 (52%)	144 (65%)	374 (57%)
Mood Stabilizer	50 (11%)	6 (3%)	56 (8%)
Benzodiazepine	46 (10%)	8 (4%)	54 (8%)
Anticonvulsant	65 (15%)	14 (6%)	79 (12%)
Other Psychotropic Agent	21 (5%)	20 (9%)	41 (6%)
Other Non-psychotropic Agent	38 (9%)	211 (96%)	249 (38%)

Table 3.7 provides statistical comparisons between the two groups. Twenty eight percent of the overall sample population (n=231) received a prescription for at least one FDA approved anti-psychotic within the study period. Approximately 32 percent of the Medicaid sample (n=174) was prescribed one or more FDA approved antipsychotics within the study period. The observed prevalence in the rural Commercial population was approximately 21 percent (n=57). The use of an approved antipsychotic was significantly greater in the Medicaid population when compared to the Commercial population (p=0.001). The overall use of Aripiprazole in the sample population was approximately 8 percent, with no significant difference observed between the Commercial and Medicaid populations (p=0.09). Approximately 20 percent of the sample population received a prescription for risperidone. Risperidone utilization was seven percent greater in the Medicaid population when compared to the rural Commercial population (p=0.009). Approximately 11 percent of the sample population (n=90) was prescribed a non-FDA approved anti-psychotic. This proportion was approximately 5% greater in the Medicaid population when compared to the Commercial population (p=0.01).

Close to sixty-two percent of the study sample was prescribed a psychotropic agent within the study period. No significant difference in overall psychotropic utilization was observed (p=0.09). Of those being treated with a psychotropic medication, on average, participants were prescribed three unique psychotropic medications within the 12 month follow-up period. One Medicaid participant was prescribed 11 unique psychotropic medications within 12 months post index; the greatest amount observed. No significant difference was observed in the average number of unique psychotropic medications prescribed to each population (p=0.09).

Four percent of the overall sample population had a confirmed medical claim from a pediatric neurologist or psychiatrist within the 12 month follow-up period. The observed proportion was significantly greater in the Texas Medicaid population when compared to the Commercial population ($p=0.008$). However, 68 percent of Medicaid claims were matched to an unknown specialty while 23 percent of claims from the Commercial sample were matched to an unknown specialty ($p<0.001$).

Table 3.7 Differences in Psychotropic Medication and Health Resource Utilization between Commercial and Medicaid Populations

Variable	**Total (N, %)**	**Medicaid (N, %)**	**Commercial (N, %)**	**P-Value**
Use of FDA approved Antipsychotic[a]	231 (28%)	174 (32%)	57 (21%)	=0.001
Use of Non-FDA approved Antipsychotic	90 (11%)	70 (13%)	20 (7%)	=0.017
Use of Aripiprazole	70 (8%)	53 (10%)	17 (6%)	=0.093
Use of Risperidone	162 (20%)	122 (22%)	40 (15%)	=0.009
Proportion of population prescribed any psychotropic medication	510 (62%)	329 (60%)	181 (66%)	=0.094
Proportion of population followed by psychiatry specialist[b]	22 (4.3%)	20 (6%)	2(1%)	=0.008
Variable	**Total (*m*[c], S.D)**	**Medicaid (*m*[c], S.D)**	**Commercial (*m*[c], S.D)**	**P-Value**
Average number of unique psychotropic medications prescribed[b]	3 (1.93)	3 (2.05)	3 (1.67)	=0.099

[a]*FDA approved Antipsychotic= Aripiprazole, risperidone*

[b]*Among those with ≥1 psychotropic prescription. Psychiatry specialist= psychiatrist, neurologist or developmental pediatrician*

[c]*m=population mean*

Result Summary

Results for all hypotheses tested are summarized in Table 3.7. Statistically significant differences were observed in all variables excluding Ho3.3, Ho3.5, Ho3.6 and Ho3.7. Over 50 percent of claims related to physician specialty contained missing or unknown values. A significant difference in the number of missing or unknown values was found between the rural Commercial and Medicaid populations ($P<0.001$).

Table 3.8 Summary of Hypotheses Tested

	Objective	P-Value	Result
Ho1.1:	When compared to a rural Commercial population, there is no statistically significant difference in the prevalence of ASD diagnoses in the Texas Medicaid population.	<0.0003	Rejected
Ho2.1:	When compared to a rural Commercial population, there is no statistically significant difference in the average age of individuals with an ASD diagnosis in the Texas Medicaid population.	<0.0001	Rejected
`1Ho3.1:	When compared to a rural Commercial population, there is no statistically significant difference in the prevalence of use of one or more FDA approved antipsychotic medications within the Texas Medicaid population.	=0.001	Rejected
Ho3.2:	When compared to a rural Commercial population, there is no statistically significant difference in the prevalence of use of one or more non- FDA approved antipsychotic medications within the Texas Medicaid population.	=0.017	Rejected
Ho3.3:	When compared to a rural Commercial population, there is no statistically significant difference in the prevalence of use of Aripiprazole within the Texas Medicaid population.	=0.093	Failed to reject
Ho3.4:	When compared to a rural Commercial population, there is no statistically significant difference in the prevalence of use of risperidone within the Texas Medicaid population.	=0.009	Rejected
Ho3.5:	When compared to a rural Commercial population, there is no statistically significant difference in the prevalence of use of any psychotropic medications within the Texas Medicaid population.	=0.094	Failed to reject
Ho3.6:	When compared to a rural Commercial population, there is no statistically significant difference in the average number of unique psychotropic medications prescribed within the Texas Medicaid population during the study period.	=0.099	Failed to reject
Ho3.7:	Among patients being treated with a psychotropic agent, when compared to a rural Commercial population, there is no statistically significant difference in the proportion of individuals being followed by a psychiatrist, neurologist, or developmental pediatrician within the Texas Medicaid population.	=0.008	Failed to reject[c]

[a] *FDA approved Antipsychotic= Aripiprazole, risperidone*
[b] *Among those with ≥1 psychotropic prescription. Psychiatry specialist= psychiatrist, neurologist or developmental pediatrician*
[c] *Significant proportion of population with missing or unknown values*

Chapter 4: Discussion and Conclusion

Discussion

This study explored the medication utilization patterns of individuals diagnosed with Autism in Texas Medicaid and Commercial populations. It also sought to describe the prevalence of ASD diagnoses within each population, the demographics of those diagnosed with an Autism Spectrum Disorder, and the rate of psychiatry follow-up among individuals prescribed a psychotropic medication.

The observed prevalence of ASD increased annually within each population. Within the study population, prevalence ranged from 0.08% to 0.5%. Though these figures are lower than the 2014 reported prevalence of 1.5%, our study results are consistent with previous publications which have reported a steady increase in the prevalence of Autism since 2008.[3,14]

In each year examined, the observed prevalence was significantly greater within the Medicaid population when compared to the rural Commercial population. This study did not aim to examine prevalence as a function of socioeconomic status. However, considering that poverty level is a criterion used in determining Texas Medicaid eligibility, it may be presumed that study participants in the Medicaid population are of a lower socioeconomic status when compared to their Commercial counterparts. In a 2012 study, Thomas et al. investigated the association of Autism diagnosis with socioeconomic status. The authors found that prevalence rates were greater among non-Hispanic whites and those with higher socioeconomic status. [12] Though the results of this study are inconsistent with those observed by Thomas et al., the observed difference in prevalence may be attributed to decreased access to mental health services in the rural central Texas region where a majority of the Commercial study population resides.

Demographic patterns observed in this study are consistent with those reported in previously published works. Specifically, the prevalence of ASDs was four times greater in the male population when compared to the female population. [3,13] In addition, the most commonly observed age at diagnosis was 4 years old.[12,13] Considering that symptoms of Autism initially present within the first three years of life, improvements in the timeliness of diagnosis may be made.

On average, individuals in the Medicaid population were approximately three years younger than those in the rural Commercial population when first diagnosed. This finding is inconsistent with previous works which have reported a greater age at diagnosis within lower income communities. [12,13] Again, this deviation from previously published results may be attributed to a relative lack of access to healthcare resources within the largely rural central Texas region.

Consistent with the findings of previous studies, stimulants, antipsychotics and anti-depressants were the most commonly prescribed psychotropic medication classes. [5,18,19,21] Stimulants were the most commonly prescribed medication class in both populations. This finding raises concerns related to the presence of confounding diagnoses such as Attention Deficit Hyperactivity Disorder within the study population. Among the Medicaid population antipsychotics were more commonly prescribed than antidepressants. Within the Commercial population, antidepressants were more commonly prescribed than antipsychotics.

Sixty-two percent of the study population received a prescription for one or more psychotropic medications within the follow-up period. This figure is consistent with previous works which have reported a psychotropic medication prevalence of 30 to 70%. [16,18,19,21-24,26] After matching on age and gender, this study found no significant difference in overall

psychotropic medication use prevalence between the two populations. On average, study participants were prescribed 3 unique psychotropic medications within 12 months following diagnosis.

Over one-fourth of the study population received a prescription for an FDA approved anti-psychotic within the follow-up period. The overall use of FDA approved antipsychotic medications was close to three times greater than that of non-FDA approved antipsychotics.

Consistent with previous studies, risperidone (20%) was more commonly prescribed in the overall population than aripiprazole (8%). [18,23] Also, risperidone use was significantly greater in the Medicaid population when compared to the Commercial population. The use of branded aripiprazole was also significantly greater in the Medicaid population. The observed difference in aripiprazole use may be attributed to the presence of fewer formulary restrictions applicable to branded medications on the Texas Medicaid formulary when compared to the Scott & White Health Plan commercial formulary. With the recent launch of generic aripiprazole, future studies may examine the resulting change in utilization of aripiprazole and risperidone within this population.

When compared to the rural Commercial population, individuals in the Medicaid population were more likely to receive antipsychotic medications. The increased use of antipsychotic medications within the Medicaid population has been documented in previous studies.[24,26] A 2005 article reported a direct correlation between antipsychotic medication use and number of psychiatric comorbidities or level of autism severity.[19,26] Since our study did not examine the number of comorbidities observed in each population examined, it may be argued that the differential use of antipsychotic medications is attributable to differences in illness severity between the study populations.

When compared to the Commercial population, a significantly greater proportion of the Medicaid population with a psychotropic prescription claim received follow-up with a psychiatrist, neurologist, or developmental pediatrician within 12 months of ASD diagnosis. Though close to 80% of Commercial provider claims were matched to a physician specialty, only 1% of those with a psychotropic prescription claim received follow-up with a psychiatrist, neurologist, or developmental pediatrician. However, since approximately 70% of provider claims within the Medicaid population returned missing or unknown physician specialties when cross referenced with the Baylor Scott & White physician directory, we are unable to reject our null hypothesis. Considering that the Baylor Scott & White physician directory includes only contracted physicians within the north and central Texas region, future studies may yield more accurate results by employing a national physician registry.

Potential Limitations

The descriptive nature of this study prohibits claims of causality. In addition, the change in ASD diagnostic criteria presented in DSM-V may limit the present day validity of results related to prevalence. To mitigate this threat, claims were reviewed from 2009 to 2012, before the change in diagnostic criteria was published. Reported prevalence rates are based on the diagnostic criteria published in DSM-IV-TR.

Inherent differences between the Medicaid and rural Commercial populations may present an additional threat to validity. To account for these differences, we matched study participants on known covariates such as age and gender to mitigate potential confounding.

The physician specialty directory utilized included only contracted physicians within the Baylor Scott & White Health System. As a result, a significant proportion of Medicaid provider specialties were not reported and we were unable to assess differences in specialist follow-up between the two populations.

It is also important to note that all study participants are Texas residents. Therefore, the generalizability of study results is limited to Texas residents with demographic characteristics similar to the study population.

Conclusion

As the prevalence of Autism and its associated costs increase, health care providers and payers must develop a broader understanding of the demographic characteristics and appropriate pharmacologic management of this population. Based on the results of this study, a significant proportion of the diagnosed population is being treated with medications that have been FDA approved for the treatment of Autism. However, despite limited evidence related to long term safety and efficacy, several off-label psychotropic medications continue to be used in this population. Results of this study also suggest a need for improvement in timely diagnosis and access to specialist care. Future studies may explore the impact of psychiatric comorbidities on the medication utilization patterns of individuals diagnosed with Autism Spectrum Disorders.

Appendix

Appendix A: Prescriptions Included in each Treatment Class

Aripiprazole	**Other Non-psychotropic Medications**
ABILIFY®	"NPH, HUMAN INSULIN ISOPHANE"
ARIPIPRAZOLE	@ARGUS COMPOUND NDC
Anticonvulsants	ACETAMINOPHEN-CODEINE
BANZEL®	ACYCLOVIR
CARBAMAZEPINE	ADAPALENE
FELBAMATE	ADVAIR DISKUS®
GABAPENTIN	ADVAIR HFA®
LACOSAMIDE	ALBUTEROL SULFATE
LAMOTRIGINE	ALLEGRA®
LEVETIRACETAM	ALLEGRA ODT®
OXCARBAZEPINE	AMLODIPINE BESYLATE
PHENOBARBITAL	AMOX TR-POTASSIUM CLAVULANATE
PHENYTOIN	AMOXICILLIN
PREGABALIN	ANTIPYRINE-BENZOCAINE
RUFINAMIDE	ATORVASTATIN CALCIUM
TOPIRAMATE	ATROPINE SULFATE
TRILEPTAL®	AZITHROMYCIN
VIGABATRIN	BACITRACIN
ZONISAMIDE	BACTROBAN

Appendix A Continued: Prescriptions Included in each Treatment Class

Antidepressants	Other Non-psychotropic Medications Continued
AMITRIPTYLINE HCL	BD ULTRA-FINE PEN NEEDLE
BUDEPRION SR	BENZACLIN
BUPROPION HCL	BENZONATATE
BUPROPION HCL SR	BENZTROPINE MESYLATE
BUPROPION XL	BETAMETHASONE VALERATE
CITALOPRAM HBR	BEYAZ®
CITALOPRAM HYDROBROMIDE	BLEPHAMIDE S.O.P.
DESVENLAFAXINE SUCCINATE	BROMDEX D®
DOXEPIN HCL	BROMFED DM®
ESCITALOPRAM OXALATE	BUDESONIDE
FLUOXETINE HCL	CEFADROXIL
FLUVOXAMINE MALEATE	CEFDINIR
IMIPRAMINE HCL	CEFPROZIL
LEXAPRO®	CEFUROXIME
PAROXETINE HCL	CELEXA®
SERTRALINE HCL	CEPHALEXIN
TRAZODONE HCL	CETIRIZINE HCL
VENLAFAXINE HCL	CHERATUSSIN AC
WELLBUTRIN XL®	CHLORAL HYDRATE
ZOLOFT®	CHLORHEXIDINE GLUCONATE
	CIPRO®

Appendix A Continued: Prescriptions Included in each Treatment Class

Benzodiazepines	**Other Non-psychotropic Medications Continued**
ALPRAZOLAM	CIPRO HC®
CLONAZEPAM	CIPRODEX®
CLORAZEPATE DIPOTASSIUM	CIPROFLOXACIN HCL
DIASTAT ACUDIAL	CLARITHROMYCIN
DIAZEPAM	CLINDAMYCIN HCL
LORAZEPAM	CLINDAMYCIN PHOSPHATE
TRIAZOLAM	CLINDAMYCIN-BENZOYL PEROXIDE
Mood Stabilizers	CLOBETASOL PROPIONATE
DEPAKOTE ER®	CLOMIPRAMINE HCL
DIVALPROEX SODIUM	CLOTRIMAZOLE
DIVALPROEX SODIUM ER	C-PHEN DM®
LITHIUM CARBONATE	CYPROHEPTADINE HCL
LITHIUM CARBONATE ER	DALLERGY PE®
LITHIUM CITRATE	DESMOPRESSIN ACETATE
VALPROATE SODIUM	DESONIDE
VALPROIC ACID	DICYCLOMINE HCL
	DIPHENOXYLATE-ATROPINE

Appendix A Continued: Prescriptions Included in each Treatment Class

Non-FDA Approved Antipsychotics	Other Non-psychotropic Medications Continued
ASENAPINE MALEATE	DOXYCYCLINE HYCLATE
GEODON®	DRYSOL®
HALOPERIDOL	ECONAZOLE NITRATE
HALOPERIDOL DECANOATE	ENALAPRIL MALEATE
ILOPERIDONE	EPIPEN®
LURASIDONE HCL	EPIPEN JR®
OLANZAPINE	EPIPEN JR 2-PAK®
PALIPERIDONE	ERYTHROMYCIN
QUETIAPINE FUMARATE	ERYTHROMYCIN-BENZOYL PEROXIDE
SEROQUEL®	ETODOLAC
ZIPRASIDONE HCL	FEXOFENADINE HCL
ZYPREXA®	FLOVENT HFA®
ZYPREXA ZYDIS	FLUCONAZOLE
	FLUOCINOLONE ACETONIDE

Appendix A Continued: Prescriptions Included in each Treatment Class

Other Psychotropic Medications	Other Non-psychotropic Medications Continued
AMANTADINE	FLUOCINONIDE
AMBIEN CR®	FLUTICASONE PROPIONATE
BUSPIRONE HCL	GAVILYTE-C®
CYCLOBENZAPRINE HCL	GAVILYTE-G®
ESZOPICLONE	GEMFIBROZIL
MEMANTINE HCL	GENERLAC
MIRTAZAPINE	GENTAMICIN SULFATE
NALTREXONE HCL	GLYCOPYRROLATE
PRAMIPEXOLE DIHYDROCHLORIDE	GRISEOFULVIN
RAMELTEON	HUMALOG®
ROPINIROLE HCL	HUMALOG KWIKPEN®
TIZANIDINE HCL	HUMALOG MIX 75-25 KWIKPEN®
TRAMADOL HCL	HYDROCODONE-ACETAMINOPHEN
ZOLPIDEM TARTRATE	HYDROCORTISONE
ZOLPIDEM TARTRATE ER	HYDROCORTISONE VALERATE
Risperidone	HYDROCORTISONE-ACETIC ACID
RISPERDAL	HYDROXYZINE HCL
RISPERIDONE	HYDROXYZINE PAMOATE
RISPERIDONE ODT	HYOMAX-SL®
	IBUPROFEN

Appendix A Continued: Prescriptions Included in each Treatment Class

Stimulants	Other Non-psychotropic Medications Continued
ADDERALL®	INSULIN LISPRO
ADDERALL XR®	INSULIN SYRINGE
AMPHET ASP/AMPHET/D-AMPHET	KETOROLAC TROMETHAMINE
AMPHETAMINE SALT COMBO	LACTULOSE
ATOMOXETINE HCL	LANSOPRAZOLE
CLONIDINE	LANTUS®
CLONIDINE HCL	LEVOCARNITINE
CONCERTA®	LIDOCAINE HCL VISCOUS
DAYTRANA®	LIDOCAINE-PRILOCAINE
DEXMETHYLPHENIDATE HCL	MALATHION
DEXTROAMPHETAMINE SULFATE	MEBENDAZOLE
DEXTROAMPHETAMINE-AMPHET ER	MEDROXYPROGESTERONE ACETATE
FOCALIN XR®	METFORMIN HCL
GUANFACINE HCL	METFORMIN HCL ER
INTUNIV®	METHYLPREDNISOLONE
KAPVAY®	METRONIDAZOLE BENZOATE
LISDEXAMFETAMINE DIMESYLATE	MILLIPRED®
METADATE CD®	MINOCYCLINE HCL
METHYLIN®	MUPIROCIN
METHYLIN ER	NAPROXEN
METHYLPHENIDATE	NASACORT AQ®

Appendix A Continued: Prescriptions Included in each Treatment Class

Stimulants Continued	Other Non-psychotropic Medications Continued
METHYLPHENIDATE ER	NASONEX
METHYLPHENIDATE HCL	NEOMYCIN-POLYMYXIN-HC
RITALIN LA®	NEOMYCIN-POLYMYXIN-HYDROCORT
STRATTERA®	NEULASTA®
VYVANSE®	NEXIUM®
Other Non-psychotropic Medications Continued	NIASPAN®
SUPRAX®	NITROFURANTOIN MONO-MACRO
TAMIFLU®	NORDITROPIN NORDIFLEX
TOBRAMYCIN	NOREL SR®
TRETINOIN	NOVOFINE 32
TRIAMCINOLONE ACETONIDE	NYSTATIN
VAZOBID®	NYSTOP®
VAZOTAN®	OCELLA®
VENTOLIN HFA®	OFLOXACIN
VERAMYST®	OMEGA-3 ACID ETHYL ESTERS
XOPENEX®	ONDANSETRON HCL
XOPENEX HFA®	ONDANSETRON ODT
PEG 3350-ELECTROLYTE	ONETOUCH ULTRA TEST STRIPS
	ORAPRED ODT®
	ORTHO TRI-CYCLEN LO®
	OXYBUTYNIN CHLORIDE

Appendix A Continued: Prescriptions Included in each Treatment Class

Other Non-psychotropic Medications Continued	Other Non-psychotropic Medications Continued
PENICILLIN V POTASSIUM	PROPOXYPHENE NAP-ACETAMINOPHEN
PERMETHRIN	RANITIDINE HCL
PLAN B ONE-STEP®	RECLIPSEN
POLYMYXIN B SUL-TRIMETHOPRIM	RETIN-A MICRO®
PORTIA®	SILDEC PE-DM®
PREDNISOLONE	SIMVASTATIN
PREDNISOLONE ACETATE	SINGULAIR®
PREDNISOLONE SODIUM PHOSPHATE	SPRINTEC®
PREDNISONE	STROMECTOL®
PREVIDENT®	SULFACETAMIDE SODIUM
PROAIR HFA®	SULFAMETHOXAZOLE-TRIMETHOPRIM
PROMETHAZINE HCL	SUMATRIPTAN
PROMETHAZINE-CODEINE	
PROMETHAZINE-DM	
PROMETHEGAN	

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