TREATMENT OF AUTISM SPECTRUM DISORDER WITHIN A MEDICAID-ENROLLED PEDIATRIC SAMPLE: PREVALENCE AND PREDICTORS OF PSYCHOPHARMACOLOGICAL TREATMENT

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ABSTRACT

TREATMENT OF AUTISM SPECTRUM DISORDER WITHIN A MEDICAID-ENROLLED PEDIATRIC SAMPLE: PREVALENCE AND PREDICTORS OF PSYCHOPHARMACOLOGICAL TREATMENT

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The purpose of this study was to contribute to the literature on the prevalence of psychotropic medications for youth with autism spectrum disorder within a sample of Medicaid-enrolled children and adolescents (N = 8,058) in the state of Michigan in the year 2009. Prevalence of psychopharmacological treatments, rates of polypharmacy, and the predictive value of participant, educational, and healthcare characteristics were analyzed. Results indicated that 60% of participants were prescribed a psychotropic medication, and approximately 36% received polypharmacy intervention. Older age, identifying as White, having an Asperger's diagnosis, and receiving a comorbid diagnosis were found to be associated with an increased likelihood of being prescribed psychopharmacologic intervention. County educational characteristics, specifically total number of students and student-teacher ratio, were also found to influence psychopharmacologic prescribing. Lastly, a dramatic increase in prevalence rates was identified between 2001 (32%) and 2009 (60%) for youth with autism spectrum disorder. In summary, psychopharmacologic prevalence doubled during the targeted decade in the state of Michigan, and variables outside of the scope of medical best practice were found to influence psychopharmacologic prescribing practices. Implications of study findings on future research are discussed.

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Chapter 1:

Introduction

Pervasive developmental disorders refer to a collective set of neurodevelopmental disorders, which have historically included autistic disorder, Asperger's disorder, and pervasive developmental disorder not otherwise specified (American Psychiatric Association, 2000). In the recently released fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-V; American Psychiatric Association, 2013), these diagnoses are referred to collectively as autism spectrum disorder. The disorder is characterized by marked deficits in social interaction and communication. Restricted and repetitive patterns of interests and behaviors also occur (American Psychiatric Association, 2013). Autism spectrum disorder is lifelong and highly idiosyncratic, ranging from mild differences in social nuances to severe disability (Hebert & Koulouglioti, 2010).

In the United States, one in 68 children has been identified with autism spectrum disorder (Baio, 2014). According to the Center for Disease Control and Prevention (CDC), this estimate represents a 30% increase compared to estimates reported in 2012, which indicated that one in 88 children was identified with autism spectrum disorder (Baio, 2012). The U.S. Department of Education (1999) characterizes autism as the largest growing low incidence disability. It has been hypothesized that the apparent increase in the occurrence of autism spectrum disorder can be attributed to broadening definitions of autism, increased demand and availability of services, and increased awareness of the disorder (Mash & Barkley, 2006). However, the CDC believes that a true increase in the number of individuals with autism spectrum disorder cannot be ruled out (Baio, 2014). Results of twin studies and genetic research lead many experts to agree that there is a strong genetic basis for autism spectrum disorder (Freitag, 2007; Muhle, Trentacoste,

& Rapin, 2004; Sunil, 2006); however, there are likely to be environmental or non-genetic factors influencing gene expression and severity (Inglese & Elder, 2009). Nevertheless, the increasing number of children with autism spectrum disorder requiring services is clear (Ruble, Heflinger, Renfrew, & Saunders, 2005).

Individuals with autism spectrum disorder present with heterogeneous profiles of associated behaviors (Kaplan & McCracken, 2012). Approximately 20% of individuals with autism spectrum disorder experience moderate to severe irritability (Lecavalier, 2006), which may manifest as temper tantrums and aggression. Self-injurious behaviors are also prevalent within this population, with the most common behaviors being head banging, biting, scratching, and hair pulling (Baghdadli, Pascal, Grisi, & Aussilloux, 2003). The severity of these behaviors can range from mild to severe, with the most severe behaviors having the potential to lead to functional impairment or life-threatening injury. Fifty percent of youth with autism spectrum disorder has been found to exhibit self-injurious behavior, with 15% of behaviors being described as severe (Baghdadli et al., 2003). Compulsive expression of stereotypic movements and high levels of hyperactivity are also frequently associated with the disorder (Kaplan & McCracken, 2012). These challenging behaviors highlight the need for efficient and effective treatments for youth with autism spectrum disorder.

Maladaptive behaviors associated with autism spectrum disorder significantly affect the functioning of these children within their familial and educational environments. The severity of the associated behaviors, particularly with regards to irritability, aggression, stereotypies, and self-injury, pose enormous challenges for youth, families, educators, and clinicians (McCracken et al., 2002). Behavioral and educational interventions are the cornerstone of treatment for children with autism spectrum disorder (McDougle, 1997), and behavior therapy may be

employed to reduce aggression and self-injury. However, due to the prevalence of these maladaptive behaviors, the resulting dysfunction, and the lack of response to psychosocial treatments in some children, psychotropic medications can serve as an important component of an individually tailored treatment plan (McDougle, 1997).

Psychopharmacological prescribing is evident in the history of treatment of autism spectrum disorder since it was first described by Kanner approximately 70 years ago (Mohiuddin & Ghaziuddin, 2012). More specifically, a follow-up study by Kanner (1971) indicated that 3 of 11 patients were taking psychotropic medications. Since that time, significant advances have been made in the evidence base for use of psychotropic medications to treat behaviors associated with autism spectrum disorder. Currently, no psychotropic medications hold Food and Drug Administration (FDA) approval for the treatment of this condition. However, psychotropic medications have received FDA approval for the treatment of severe symptoms associated with autism spectrum disorder, including irritability and aggression.

Specifically, two atypical antipsychotics have been approved by the FDA for the treatment of irritability associated with autism spectrum disorder. A series of randomized controlled trials support the efficacy, safety, and tolerability of risperidone (McCracken et al., 2002; McDougle et al., 1998; Shea et al., 2004; Troost et al., 2005) and aripiprazole (Aman et al., 2010; Marcus et al., 2009; Owen et al., 2009) among individuals with autism spectrum disorder. Risperidone became FDA approved in 2006, followed by aripiprazole in 2009 (Mohiuddin & Ghaziuddin, 2012). As such, the research literature suggests that irritability and aggressive behavior associated with autism spectrum disorder can be effectively treated with psychopharmacological intervention.

In addition to the use of atypical antipsychotics for the treatment of irritability, several other classes of psychotropic medications are prevalent in the treatment of symptoms associated with autism spectrum disorder. Antidepressants, stimulants, anxiolytics, and anticonvulsants have all been reported as possible treatments for associated symptoms (Canitano & Scandurra, 2011; Handen & Lubetsky, 2005; Kaplan & McCracken, 2012; King, 2000; Mohiuddin & Ghaziuddin, 2012; Nazeer, 2011; Siegel & Beaulieu, 2012). However, they remain largely unsubstantiated through clinical trials within populations of individuals with autism spectrum disorder.

Interest in the prevalence of psychopharmacological prescribing within this population increased beginning in 1995. Recognition of common treatment methods for behaviors associated with autism spectrum disorder allows clinicians and researchers to identify commonly used treatments and respond accordingly within clinical practice. Furthermore, prevalence studies also have utility for the identification of variables that may contribute to utilization of treatment practices, such as demographic, educational, or healthcare characteristics across geographic regions. Together, statistics yielded within prevalence studies and the identification of predictive variables that influence those statistics can provide valuable information to clinicians during consideration of comprehensive treatment plans for individuals with complex mental health needs.

Four prevalence studies of psychotropic prescribing have been completed for populations of individuals with autism spectrum disorder. The first investigation of psychopharmacological prevalence occurred in 1995 within a sample of individuals of diverse age groups who were members of the Autism Society of North Carolina. The study revealed that 39% of participants with autistic disorder were taking at least one psychotropic medication (Aman, Van

Bourgondien, Wolford, & Sarphare, 1995). The second study, which also consisted of families who were members of the Autism Society of North Carolina (Langworthy-Lam, Aman, & Van Bourgondien, 2002), and the third study, which consisted of families who were members of the Autism Society of Ohio (Aman, Lam, & Collier-Crespin, 2003), both yielded prevalence rates of approximately 46%. The fourth investigation of psychotropic prevalence rates indicated that 56% of a national sample of Medicaid-enrolled youth was prescribed psychopharmacologic intervention (Mandell et al., 2008).

Of note, increases in the prevalence of psychotropic prescribing among populations of individuals with autism spectrum disorder were observed across these different studies between 1995 and 2003. Similarly, rates of individuals with autistic disorder who were taking two or more concurrent psychotropic medications increased from 9% (Aman et al., 1995) to 21% between 1995 and 2003 (Aman et al., 2003), indicating an increase in the prevalence of polypharmacy intervention over time. Although rates of polypharmacy intervention appear to be increasing, there is a dearth of research regarding the use of multiple, concurrent psychotropic medications within developing children.

Additional contributions of these prevalence studies included identification of the classes of medications that are most commonly prescribed for youth with autism spectrum disorder. Differences in the most commonly prescribed medication classes were observed across studies. While antidepressants were the most commonly prescribed classes in the studies by Langworthy-Lam et al. (2002) and Aman et al. (2003), antipsychotic agents were identified as the most commonly prescribed agents by Aman et al. (1995) and Mandell et al. (2008). Other than those agents that have received FDA approval (i.e., risperidone, aripiprazole), the literature suggests

that other prescribing practices have preceded solid scientific evidence of their efficacy and safety within youth with autism spectrum disorder.

Of the four prevalence studies to date, it is important to recognize limitations present within the literature. Only one study focused exclusively on child and adolescent participants (Mandell et al., 2008). Furthermore, only one study examined psychotropic medication use within early childhood (Mandell et al., 2008). Although the most recent prevalence study was published in 2008, it focused on prescribing practices from the year 2001. Given the number of randomized control trials of psychotropic medications and the FDA approval of two atypical antipsychotic since the year 2000, additional investigations of psychopharmacological prevalence among populations with autism spectrum disorder is warranted. Additionally, three of the previous studies (Aman et al., 1995; Aman et al., 2003; Langworthy-Lam et al., 2002) included state-level investigations, whereas the fourth provided contributions examining a national sample (Mandell et al., 2008). To date, no studies have examined psychotropic prescribing practices exclusively in the state of Michigan.

The general perception of the epidemiological characteristics of autism spectrum disorder is that "Autism…knows no racial, ethnic, or social boundaries. Family income, lifestyle, and educational levels do not affect the chance of autism's occurrences" (Autism Society of America, 2000, p. 3). Despite autism spectrum disorder occurring equitably across epidemiological characteristics, many of these variables have been found to have predictive effects on psychopharmacological prescribing practices for youth with autism spectrum disorder. Prior research has suggested that variables at the participant, demographic, and educational levels may influence psychopharmacological prescribing practices.

For example, age has been found to influence psychotropic prevalence rates for individuals with autism spectrum disorder. Greater age has been found to be predictive of increased use of psychotropic medications (Aman et al., 1995; Aman et al., 2003; Langworthy-Lam et al., 2002; Mandell et al., 2008), as well as use of particular psychotropic agents (Aman et al., 1995; Langworthy-Lam et al., 2002). Older children have been found to be more likely to be prescribed antipsychotic medications (Aman et al., 1995; Langworthy-Lam et al., 2002), whereas younger children have been found to be more likely to be prescribed stimulant medications (Langworthy-Lam et al., 2002).

Gender has been also been found to be predictive of psychopharmacological prescribing practices, with low-income males being more likely to receive psychotropic medications compared to low-income females (Mandell et al., 2008). However, the gender distribution within the samples of previous studies is consistent with the gender-related features of autism spectrum disorder, with rates of the disorder being four to five times higher in males than in females (American Psychiatric Association, 2000). Moreover, studies of general psychopharmacologic prescribing have indicated that males are more likely to receive psychotropic medications (Martin, Van Hoof, Sherwin, & Scahill, 2003). Gender effects have been notably inconsistent across research studies regarding individuals with autism spectrum disorder; therefore, further research is needed in order to determine the predictive value of gender on psychopharmacological prescribing within this population.

Research has also suggested that race and ethnicity is associated with differences in psychopharmacological prescribing practices for individuals with autism spectrum disorder. White children have been found to be more likely to receive psychotropic medications than their African American (Hahn, 1995; Martin et al., 2003; Zito et al., 1998), Asian (Mandell et al.,

2008), and Hispanic (Martin et al., 2003; Hahn, 1995) counterparts. General studies of psychopharmacology have also indicated that African American youth are less than half as likely to receive psychopharmacological treatments compared to White children ages 5 to 14, even when controlling for geographic variability (Zito et al., 1998). Although autism spectrum disorder occurs equitably across demographic groups, decreased access to healthcare services may lead to under identification of the disorder and/or underutilization of mental health care services.

The common presence of comorbid diagnoses adds another layer of complexity to the clinical profiles of children with autism spectrum disorder. There is a high prevalence of inattentive and hyperactive symptoms, with research indicating that 28% to 78% of children with autism spectrum disorder meet diagnostic criteria for attention-deficit/hyperactivity disorder (Murray, 2010). In addition, symptoms of anxiety and depression are present in many children and adolescents with autism spectrum disorder (Mayes, Calhoun, Murray, & Zahid, 2011), with estimates of comorbid depression ranging from 4% to 38% (Lainhart, 1999). Depression is especially common in adolescence and adult life for those individuals with autism spectrum disorder who have the intellectual capacity to recognize their level of impairment (American Psychiatric Association, 2000). Additionally, the majority of cases with a historical diagnosis of autistic disorder have an associated diagnosis of intellectual disability (Mash & Barkley, 2006). Seizure disorders are also common within 25% of cases of autistic disorder, with seizures most commonly presenting in adolescence (American Psychiatric Association, 2000).

Given the high prevalence of comorbid psychiatric diagnoses for youth with autism spectrum disorder, the effects of comorbid diagnoses on psychopharmacological prescribing practices have been noted within the research literature. Comorbid intellectual disability predicts

greater use of psychotropic agents (Aman et al., 1995; Aman et al., 2003; Langworthy et al., 2002), with psychotropic prescribing being positively correlated with increasing severity of intellectual disability (Mandell et al., 2008). In addition, anxiety and depression have been found to be more prevalent in individuals of greater age and higher intellectual level, variables which have been found to influence psychotropic prevalence rates (Martin et al., 2003).

In addition to the effects of individual-level characteristics on psychopharmacological prescribing practices, it has been suggested that county-level demographic characteristics may have a significant influence on psychopharmacological prescribing practices. For instance, community demographics, such as percentage of the community with low socioeconomic status, urban environments, greater percentages of White residents, and lower levels of parental education, have been found to influence psychotropic prevalence rates for individuals with autism spectrum disorder (Langworthy et al., 2003; Liptak et al., 2008; Mandell et al., 2008).

Lastly, county educational characteristics may also play an influential role in psychopharmacological prescribing practices. Counties in which there are greater proportions of students receiving special education services have been associated with a greater number of Medicaid-enrolled children, which may positively influence access to healthcare (Mandell et al., 2010) and utilization of various treatment approaches. As result, county educational characteristics, such as the proportion of students in special education, the total number students served, and pupil/teacher ratios, have the capacity to influence psychopharmacological prescribing practices for this population.

In summary, the research literature has indicated an increase in psychopharmacologic prescribing and polypharmacy intervention for youth with autism spectrum disorder in the early 2000s. However, prevalence studies predate significant advances in the research surrounding the

efficacy, safety, and tolerability of psychotropic medications for youth with autism spectrum disorder. Additional investigations of psychopharmacologic prescribing within this population are warranted. Furthermore, it has been suggested that variables beyond the scope of medical best practice, such as individual, demographic, and educational characteristics, may influence psychopharmacological treatment practices. Further research is needed to more completely understand factors that play a role in comprehensive treatment plans for youth with autism spectrum disorder.

The purpose of this study was to contribute to the literature on the prevalence of psychotropic medications for youth with autism spectrum disorder within a sample of Medicaid-enrolled children in the state of Michigan. Prevalence rates of psychopharmacological treatments and polypharmacy were analyzed using insurance claims from the 2009 calendar year. Given the calendar year associated with the data set, autism spectrum disorder was categorized according to pervasive developmental disorder diagnoses outlined in the fourth edition of the diagnostic and statistical manual of mental disorders (APA, 2000). The predictive value of individual characteristics, including age, gender, race/ethnicity, autism spectrum disorder diagnosis, and presence of psychiatric comorbidities, on psychopharmacological prescribing was investigated. The effect of county demographic, educational, and healthcare characteristics on psychopharmacological prescribing practices was also examined. Lastly, changes in psychopharmacological prevalence rates were analyzed between 2001 and 2009, a time period of considerable advances in the treatment of individuals with autism spectrum disorder.

Chapter 2:

Literature Review

The following literature review provides an overview of autism spectrum disorder and the biopsychosocial theoretical model that supports the present study. Subsequently, the research regarding the safety, efficacy, and tolerability of psychopharmacological treatments for the behaviors associated with autism spectrum disorder are discussed. The state of the evidence regarding the prevalence of psychopharmacological prescribing for this population was reviewed. In addition, variables that may serve to influence psychopharmacological prescribing practices are highlighted. Lastly, the purpose of the current study, research questions, and hypotheses that drive the study are presented.

Autism spectrum disorder, previously known as a series of pervasive developmental disorders, is a neurodevelopmental disorder that is characterized by marked impairments in reciprocal social interaction and communication skills, as well as by the presence of stereotyped patterns of behaviors and interests. Qualitative impairments in these areas span beyond what is expected based on intellectual level and mental age. These disorders are evident in the first years of life and persist throughout the lifespan. Autism spectrum disorder frequently co-occurs with varying degrees of intellectual disability (American Psychiatric Association, 2000).

In the recent release of the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5) (American Psychiatric Association, 2013), pervasive developmental disorders were placed under the broader category of autism spectrum disorder. This literature review will include the previously identified subtypes of pervasive developmental disorders outlined in the fourth edition of the DSM (American Psychiatric Association, 2000) for consistency with prior research literature. While these disorders share similar core characteristics, important distinctions

separate them. The criteria for autistic disorder include a delay or abnormal functioning in social interaction, language, and symbolic or imaginative play prior to three years of age. In contrast, no clinically significant delays in language use, cognitive development, or adaptive skills are observed for individuals with Asperger's disorder. Furthermore, individuals with Asperger's disorder display fewer deficits in communication. While all of the aforementioned diagnoses have been combined in the recent release of the DSM-V (American Psychiatric Association, 2013), differences in clinical presentation and required levels of care persist.

In addition to the core symptoms of autism spectrum disorder, individuals with this disorder present with a variety of associated behaviors. Behaviors that are frequently associated with these disorders include hyperactivity, inattention, irritability, aggression, and self-injurious behavior (Kaplan & McCracken, 2012). While a repertoire of associated behaviors can be identified, behavioral profiles are highly idiosyncratic. Individuals with this disorder may also have atypical responses to sensory stimuli (e.g., oversensitivity to light or sound, high threshold for pain) and abnormalities in mood (e.g., unprovoked laughing or crying) (American Psychiatric Association, 2013).

No cure exists for autism spectrum disorder. Behavioral and educational interventions are the hallmark of treatment for the core deficits of this disorder (McDougle, 1997). While many effective behavioral and educational approaches exist, these treatments require large levels of client participation. The presence of associated behavioral challenges can limit developmental progress and treatment success (Aman et al., 2005). Many of these severe behaviors can lead to harm to the individual, to caregivers, and to service providers, as well as significantly affect quality of life (Owen et al., 2009). When used judiciously and in combination with behavioral

and educational treatments, psychotropic medications can play an integral role in comprehensive care for individuals with autism spectrum disorder (Mohiuddin & Ghaziuddin, 2012).

Theoretical Perspective

The theoretical model of treatment of autism spectrum disorder driving this study is the biopsychosocial model. Originally posited by Engel (1977), the biopsychosocial model provides a blueprint for research, a framework for teaching, and a design for action in the real world of healthcare. The biopsychosocial model suggests that health is best understood in terms of the influences between the biological, psychological, and social factors that play significant roles in human functioning. This model was proposed in contrast to the biomedical model, which focuses solely on the physiology of illness and leaves no room for the social, psychological, and behavioral dimensions of illness. It proposes that disease and mental health are not qualitatively different, such that both can arise from specific biochemical abnormalities that are capable of being influenced pharmacologically. While biological, psychological, and social factors are independent, they are also interrelated and affect the manifestation of the disease and variations in its course (See Figure 1).

Standards of care for children with autism spectrum disorder have been outlined in order to guide publicly funded agencies. Children with autism spectrum disorder benefit from proactive behavioral management, positive reinforcement systems, social skills training, speech and language therapy, and less traditional services, such as respite (American Academy of Pediatrics, 2001; Committee on Children with Disabilities, 2001; National Research Council, 2001). The National Autism Center (2009) recommends a biopsychosocial model of treatment for autism spectrum disorder, which encourages the use of the aforementioned educational, environmental, and behavioral modification strategies in conjunction with biomedical

psychopharmacological practices. Care guidelines include comprehensive and intensive early intervention services that address biomedical, psychological, and social influences on the individual.

While agreement has been reached regarding best practices for young children with autism spectrum disorder, research on the service delivery system for this population is lacking (Ruble et al., 2005). The absence of data regarding service delivery makes it extremely difficult to study the implementation of best practices, examine the methods that bridge the gap between research and practice, or promote the management of long-term outcomes (Perrin, 2002). While some attention has been paid to improving care for youth with autism spectrum disorder who are covered by commercial insurance, Medicaid's role in delivering services to this population has received much less consideration (Semansky, Xie, & Mandell, 2011).

Medicaid, which is a jointly funded state and federal health program for the economically disadvantaged and disabled, is the largest single public payer of behavioral health services (Mark, Buck, Dilonardo, Coffey, & Chalk, 2003). It is a pertinent financial resource for individuals with developmental disabilities, accounting for 75% of all funding for related services (Braddock, Hemp, Rizzolo, Parish, & Pomeranz, 2002). National estimates indicated that approximately 95,900 youths within the Medicaid system have an autism spectrum disorder diagnosis (Semansky et al., 2011). A study of behavioral health utilization conducted in a Medicaid managed care program in Tennessee found that the number of children with autism spectrum disorder who received services over time increased significantly between 1995 and 2000. Moreover, the observed increase in service provision was only half of what should be expected based on increasing prevalence rates. Still further, medication and case management increased disproportionately to the number of children served (Ruble et al., 2005).

While more research is needed in this area, what is known about Medicaid service provision indicates that despite the increasing need for behavioral health services among populations with autism spectrum disorder, levels of service have been unable to meet the needs of these individuals. Furthermore, this may pose a challenge regarding the implementation of the biopsychosocial model of treatment that was recommended by the National Autism Center (2009), with reported decreases in individual therapy and increases in biomedical interventions (Semansky et al., 2011). Issues related to health care utilization are particularly relevant in the state of Michigan, as legislature continues to work on revising health care policies for youth with autism spectrum disorder.

Psychopharmacology for Maladaptive Behaviors Associated with Autism Spectrum Disorder

No effective psychopharmacological treatments are available for the core symptoms of autism spectrum disorder (i.e., communication deficits, poor social interactions) (Canitano & Scandurra, 2011; Handen & Lubetsky, 2005; Kaplan & McCracken, 2012; King, 2000; Mohiuddin & Ghaziuddin, 2012; Nazeer, 2011; Siegel & Beaulieu, 2012). However, randomized controlled trials have demonstrated the efficacy of psychopharmacological treatment options for behaviors frequently associated with autism spectrum disorder, such as irritability, aggression, hyperactivity, and repetitive thoughts and behaviors (Kaplan & McCracken, 2012). Psychopharmacological treatment options emerged as biomedical studies indicated differences in the neurochemical presentation of individuals with autism spectrum disorder, which will be further described in the following section.

State of the Evidence for Psychotropic Medications for Children with Autism Spectrum Disorder

Biomedical research regarding the neurochemistry of individuals with autism spectrum disorder has fueled research regarding psychopharmacological agents that have the potential to affect the behaviors associated with these disorders. Several researchers and research groups have highlighted the efficacy and tolerability of psychopharmacological practices for maladaptive behaviors associated with the diagnosis, such as aggression, irritability, self-injury, repetitive behaviors, and hyperactivity (See Table 1.) (Canitano & Scandurra, 2011; Handen & Lubetsky, 2005; Kaplan & McCracken, 2012; King, 2000; Mohiuddin & Ghaziuddin, 2012; Nazeer, 2011; Siegel & Beaulieu, 2012). This review of the literature will focus exclusively on the studies demonstrating the most methodological rigor and will only include randomized controlled trials of psychotropic agents. Relevant medication classes include atypical antipsychotics, antidepressants, stimulants, norepinephrine reuptake inhibitors, alpha-2 adrenergic agonists, and anticonvulsants. The most researched individual agents within each medication class are also presented in Table 2.

Atypical Antipsychotics

According to Campbell, Anderson, and Small (1990), autism was once conceptualized as an early manifestation of schizophrenia. As a result, antipsychotic drugs, which treat symptoms of psychosis, were among the first medications to be prescribed among youth with autism spectrum disorder (Mohiuddin & Ghaziuddin, 2012). The antipsychotic drugs chlorpromazine, thioridazine, and haloperidol have been associated with early treatment of these disorders (Campbell et al., 1990). Haloperidol, a potent postsynaptic dopamine-receptor antagonist, may still be prescribed for youth who are unresponsive to atypical antipsychotics, although it is prescribed less frequently (Mohuiddin & Ghaziuddin, 2012). In recent years, atypical antipsychotics are more prevalent than traditional antipsychotics due to the intense side effects

that have been associated with traditional neuroleptics (Anderson, Campbell, Adams, Small, Perry, & Shell, 1989), with a study reporting that 34% of participants in a study of haloperidol presented with drug-related dyskinesias (Campbell, Armenteros, Malone, Adams, Eisenberg, & Overall, 1997). Research evidence supports the use of two atypical antipsychotics, risperidone and aripiprazole, to improve maladaptive behaviors associated with autism spectrum disorder (See Table 3.).

Risperidone. The use of atypical antipsychotics is of interest to researchers after the lack of efficacy seen with conventional antipsychotics for the treatment of adults with schizophrenia, in addition to the presence of extrapyramidal side effects. Risperidone, an atypical antipsychotic, functions by blocking postsynaptic dopamine and serotonin receptors (Glick, Murray, Vasudevan, Marder, & Hu, 2001). However, atypical antipsychotics may be more easily displaced by endogenous dopamine, leading to fewer neurological side effects that can result from the use of conventional antipsychotics (Kapur & Seeman, 2001). Due to the success of risperidone in treating adults with schizophrenia and approval by the Food and Drug Administration (FDA) in 1993, risperidone became an agent of interest for conditions with severe behavioral disturbances that require use of neuroleptics, such as autism spectrum disorder (Aman & Madrid, 1999; Kaplan & McCracken, 2012).

The first randomized, double-blind, placebo-controlled study of the efficacy and safety of risperidone use in children with autistic disorder was conducted by the Autism Network of the Research Units on Pediatric Psychopharmacology (RUPP) (2002). The study employed a placebo parallel design across five university-based sites with a sample of 101 children and adolescents. Age of participants ranged from 5 to 17, with each participant meeting criteria for autistic disorder according to the DSM-IV-TR (American Psychiatric Association, 2000).

Eighty-two participants were male and 19 were female. Participants were required to receive a score of 18 or higher on the Irritability subscale of the Abberant Behavior Checklist (ABC) according to parent report, which includes questions regarding aggression, self-injury, tantrums, agitation, and unstable mood.

Participants were randomly assigned to receive risperidone at a dosage ranging from 0.5 to 3.5 milligrams per day or placebo over a period of 8 weeks. Risperidone dosage was determined according to child weight. The primary outcome measures were the parent-rated Irritability subscale of the ABC and the Improvement rating on the Clinical Global Impressions (CGI) assessment, which was determined by the clinical evaluator. Scores on the Social Withdrawal, Stereotypy, Hyperactivity, and Inappropriate Speech subscales of the ABC-I served as additional measures of treatment outcomes.

Results of the study indicated a significant interaction between treatment group and time according to the ABC, with the risperidone group exhibiting a 57% decrease in the mean Irritability score compared to a 14% decrease in the placebo group. The study also investigated positive responses across groups as operationalized by a 25% improvement on the Irritability subscale score of the ABC and a rating of "much improved" or "very much improved" on the CGI improvement rating. Sixty-nine percent of the risperidone group exhibited positive responses, as compared to 12% in the placebo group. Risperidone reduced stereotyped behavior and hyperactivity, but it did not significantly reduce social withdrawal or inappropriate speech.

While the RUPP (2002) study suggests that positive outcomes are related to risperidone use for the aggressive behaviors associated with autistic disorder in children and adolescents, the study also recorded adverse events associated with the medication. However, most adverse events were mild. Motor-related side effects were assessed weekly for children within both

groups using the Abnormal Involuntary Movement Scale and the Simpson-Angus scale. Neither group demonstrated extrapyramidal symptoms, but five neurologic side effects were reported, including abnormal or impaired voluntary movement (dyskinesia), rigidity, motor restlessness (akathisia), difficulty swallowing, and tremor, with tremor being significantly more common within the experimental group. While no serious adverse events were documented in the risperidone group and no children withdrew from the study due to adverse effects, the study reported increased appetite, fatigue, and drowsiness within the treatment group. Most symptoms of fatigue subsided over the course of treatment. Taking into consideration efficacy versus adverse effects, the authors of the study suggest that the risk-benefit ratio for risperidone use is favorable, and they concluded that risperidone was safe and effective for short-term treatment of irritability and aggression in children with autistic disorder.

At the conclusion of the 4-month open-label treatment portion of the study, RUPP (2005) built upon the original study in order to determine if short-term efficacy and tolerability would endure over time, as well as to examine the feasibility of discontinuation. A randomized, double-blind, placebo-substitution study of risperidone withdrawal was conducted. The sample consisted of 32 patients who showed a positive response to risperidone treatment in the original study. The participants were randomly assigned to risperidone at the same dose or a gradual placebo discontinuation. Patients participating in part one and two of the study underwent six months of total drug exposure, with a placebo-controlled discontinuation period of 8 weeks. The researchers define relapse as a 25% increase in score on the parent-rated Irritability subscale of ABC and a CGI improvement rating of “much worse” or “very much worse” for two consecutive weeks as compared to the prediscontinuation baseline.

The RUPP (2005) extension study yielded statistically significant results, with a 63% relapse rate for gradual placebo substitution versus 13% for continued risperidone use. Gradual substitution of placebo for risperidone was associated with a rapid return of aggression, temper outbursts, and self-injurious behavior during the discontinuation phase. Furthermore, the improvements on the ABC subscales for hyperactivity, stereotypic behavior, and lethargy/social withdrawal were maintained for participants who continued risperidone treatment. The mean reduction of 59% in the ABC Irritability subscale score found from baseline to the last observation of the extension phase was strikingly similar to that observed at the completion of the 8-week double-blind efficacy trial for the risperidone group, providing additional support for the efficacy of risperidone treatment for short-term and intermediate-term management of serious behavioral problems in youth with autistic disorder. This two-part study was a considerable contribution to the research literature on the treatment of problem behaviors associated with autistic disorder using atypical antipsychotics.

The third study evaluating the efficacy of risperidone treatment to treat disruptive behaviors associated with autism spectrum disorder in youth was a randomized, double-blind, placebo-controlled trial conducted over multiple sites in Canada (Shea et al., 2004). A sample of 79 children ages five to 12 underwent eight weeks of risperidone or placebo. In contrast to the RUPP (2002) study, inclusion criteria included any DSM-IV-TR (APA, 2000) diagnosis of a pervasive developmental disorder and a score of 30 or more on the Childhood Autism Rating Scale (CARS) (Schopler, Reichler, & Renner, 1985). In addition, no criteria for baseline levels of irritability were required. The mean age of participants was 7.5 years. The majority of participants had a diagnosis of autistic disorder (70%), with 15% of the remaining participants having a diagnosis of Asperger's disorder, 1% having childhood disintegrative disorder, and 14%

having a pervasive developmental disorder not otherwise specified. The majority of the participants had mild to moderate intellectual disability.

After accounting for attrition, the analysis consisted of a risperidone group of 39 participants and a placebo group of 38 participants. The mean dose of risperidone was 1.17 milligrams per day, or 0.04 milligrams per kilogram per day. At the end of the study, ratings on the primary outcome measure (ABC Irritability subscale) for the risperidone group suggested a 64% improvement, which was more than double the improvement documented for the placebo group (31%). According to results on the ABC subscales, significant reductions were found for lethargy and social withdrawal, stereotypic behavior, hyperactivity and noncompliance, and inappropriate speech (Aman & Singh, 1986). Eighty-seven percent of the risperidone group exhibited significant global improvement compared to 40% in the placebo group according to the Clinical Global Impressions Change scale. Further positive outcomes were found for the conduct problems, insecure/anxious, hyperactive, and overly sensitive subscales on the Nisonger Child Behavior Rating Form (N-CBRF).

As seen within the RUPP (2002) study, the Shea et al. (2004) study reported that risperidone was well-tolerated. The most frequently reported adverse effects were somnolence, upper respiratory tract infection, rhinitis, increased appetite, and abdominal pain. Somnolence resolved naturally, through dose-modification, or dose scheduling modification in 86% of participants reporting this effect. Again, weight gain within the risperidone group was greater than that of the placebo group, with gains of 2.7 kilograms and 1.0 kilogram, respectively. No significant differences were found between the groups for extrapyramidal symptoms based on the post-baseline mean. Despite the limitation of a short treatment interval, the use of risperidone was a safe and efficacious treatment option for disruptive behaviors associated with autism

spectrum disorder. The weight gain observed within both studies warrants the institution of a dietary regimen and an exercise plan as a preventative measure. However, previous research regarding longer-term use of risperidone suggests that weight gain is more prominent in the first months of therapy (Turgay, Binder, Snyder, & Fisman, 2002).

The fourth study examined the long-term efficacy of risperidone utilizing a placebo discontinuation research design (Troost et al., 2005). Primary inclusion criteria included children ages 5 to 17 with a DSM-IV-TR (American Psychiatric Association, 2000) diagnosis of a pervasive developmental disorder, which includes autistic disorder, Asperger's disorder, or a pervasive developmental disorder not otherwise specified. Participants also needed to demonstrate clinically significant tantrums, aggression, self-injurious behavior, or a combination of these behaviors as evidenced by clinician ratings of moderate or higher on the disruptive behavior portion of the CGI Severity scale (CGI-S) and according to parent- and clinician-report on the Irritability scale of the ABC.

Thirty-six children met inclusion criteria for the study and began an 8-week open-label treatment with risperidone. Only short-term responders to risperidone during the first eight weeks of treatment could complete the research protocol, defined as at least a 25% improvement on the Irritability subscale of the ABC and a rating of “much improved” or “very much improved” on the Severity scale of the CGI. Twenty-six participants were considered responders under this criteria and continued treatment for 16 weeks, with two participants discontinuing treatment due to excessive weight gain. This period was followed by a double-blind discontinuation study with a discontinuation group who received three weeks of medication tapering and five weeks of placebo. Within the study, relapse was defined as the CGI Symptom Change scores of “much worse” or “very much worse” for at least two consecutive weeks

compared to baseline of the continuation phase, as well as a minimum increase of 25% on the ABC Irritability subscale.

Results of the 24 weeks of open-label treatment suggest that all 26 participants demonstrated at least minimal improvement, with 18 of the 26 participants receiving a "much improved" or "very much improved" rating on the CGI Symptom Change scale. According to the ABC, the most improvement occurred within the first 8 weeks. Within the discontinuation phase, 3 of the 12 participants randomized to risperidone treatment experienced relapse as compared to 8 of the 12 participants randomized to the placebo group. Differences in relapse were evidenced by a 60% increase on the ABC Irritability subscale versus 14% in patients in the treatment group. The participants in the risperidone group also exhibited a longer mean time of relapse. While overall improvement was seen within the risperidone group, positive effects attenuated over time in about half of the participants, which may point to the need to modestly increase dosage after the first several months in order to achieve enduring effects. Similar to previous studies, risperidone was well tolerated and all side effects were mild to moderate. No withdrawal effects were observed during the discontinuation phase.

The results of this randomized, double-blind, placebo-discontinuation study provided further support for the long-term effectiveness of risperidone in low and intermediate doses. These findings are commensurate with the RUPP (Aman et al., 2005; McCracken et al., 2002) studies. Furthermore, the Troost et al. (2005) study demonstrated the effectiveness of risperidone in treating tantrums, aggression, and self-injurious behavior for a broader range of children and adolescents on the autism spectrum, including those with Asperger's disorder and pervasive developmental disorder not otherwise specified. In contrast with the previous RUPP study, the Troost et al. (2005) found a relapse rate that was two times higher, which may be attributable to

the open-label nature of the initial treatment phase. Another finding that differed from previous research included significantly lower ratings on the Social Withdrawal subscale of the ABC at 24 weeks of treatment, which indicates that risperidone may have contributed to improvements in this area.

An additional contribution from the Troost et al. (2005) study was that although the relapse rate was significantly higher in the placebo group, one third of the participants in the placebo group received stable ratings during the discontinuation period. This finding suggests that risperidone may have a stabilizing effect even after medication discontinuation. However, this finding must be interpreted with caution, as a placebo effect during the treatment phase or other extraneous variables may account for this finding. Nonetheless, this finding is important when considering the long-term use of risperidone as it indicates that some long-term users of risperidone can safely be withdrawn from the medication with enduring positive effects.

While the Troost et al. (2005) study remains a significant contribution to the treatment of behaviors associated with autism spectrum disorder using psychopharmacological treatments, several limitations were present. First, the mean age of participants was nine years and 90% of the sample was male, which limits generalizability to female children and adolescents. Second, the sample consisted predominantly of high functioning children, with 50% of the risperidone group and 75% of the placebo group having average or above average intelligence. Third, approximately 21% of all participants across groups were receiving concomitant medications, including stimulants or a combination of stimulants and anticonvulsants. It is uncertain how the presence of concomitant medications could have affected the research findings.

In summary, the efficacy, safety, and tolerability of risperidone led to FDA approval of the drug for irritability associated with autism spectrum disorder in 2006. Despite this fact,

several limitations exist within the state of the research regarding this psychopharmacological agent. A paucity of research continues to exist related to intermediate- and longer-term use. Moreover, research regarding minimal effective dose is not present within the literature. While this appears to be an efficacious treatment for irritability, these questions serve as future directions for research.

Aripiprazole. Aripiprazole is the second atypical antipsychotic to receive FDA approval for irritability associated with autistic disorder. Irritability may manifest as tantrums, aggression, and self-injurious behavior within populations of youth with autism spectrum disorder. The first study to examine the safety and efficacy of aripiprazole within this population through a randomized controlled trial was conducted by Owen and colleagues (2009). A randomized 8-week, double-blind, placebo-controlled, parallel-group study was conducted on a sample of 98 children and adolescents ages 6 to 17. Participants received flexible doses of aripiprazole ranging from 5 to 15 milligrams per day.

According to the Irritability subscale of the ABC, aripiprazole was found to be significantly superior to placebo starting in the first week of treatment, with superiority persisting until week 8. Significantly greater global improvement was observed in the treatment group according to the mean CGI Improvement score across all 8 weeks. Positive results on the hyperactivity, stereotypy, and inappropriate speech subscales of the ABC were associated with use of this agent, suggesting additional benefits of the agent for these behaviors. Improvements in overall quality of life were also documented through the Pediatric Quality of Life Inventory (PedsQL) and the Caregiver Strain Questionnaire (CGSQ).

Fatigue, somnolence, and weight gain were the most commonly reported side effects associated with aripiprazole treatment. Extrapyramidal symptoms did occur within the treatment

and placebo groups, with percentages of 15% and 8%, respectively. No adverse events were serious in nature. The resulting adverse event statistics suggest that aripiprazole is generally well-tolerated within children and adolescents with autistic disorder in the short-term. Long-term studies have yet to be conducted.

A second, larger scale study investigating the efficacy of aripiprazole was conducted in the same year on 218 children and adolescents with autistic disorder and associated irritability (Marcus et al., 2009). Participants, ranging in age from 6 to 17, were randomly assigned in a 1:1:1:1 ratio of placebo or 5, 10, or 15 milligrams of the agent over a period of 8 weeks in a double-blind, placebo-controlled, parallel-group study. Results indicate that significant improvements were observed in the treatment group over the control group according to caregiver ratings on the Irritability subscale of the ABC. At week 8, Clinician Improvement scores on the CGI suggested significantly greater improvement in the treatment group. Generally, the participants experienced rapid improvements, with statistically greater improvement starting in week 2 of treatment, at which time all treatment participants were receiving 5 milligrams of aripiprazole.

Consistent with the results of the Owen et al. (2009) study, sedation was the most common adverse event leading to discontinuation in the Marcus et al. (2009) study. Extrapyramidal symptoms were reported as adverse events, with the most common symptoms being tremor and akathisia. An additional consistent finding with the previous study was the presence of weight gain. Although no serious adverse events were associated with aripiprazole use in the prior study, two serious adverse events occurred, which included presyncope and aggression. Overall, the authors concluded that aripiprazole was efficacious in the short-term and a well-tolerated treatment for irritability associated with autistic disorder.

The final randomized controlled trial investigating the efficacy of aripiprazole to date consisted of two 8-week, double-blind, multicenter trials on youth with autistic disorder ages 6 to 17 (Aman et al., 2010). Participants received a flexible dose (2-15 mg/day) or a fixed dose (5, 10, or 15 mg/day) of aripiprazole. All treatment arms of the study led to significant reductions in Irritability, Stereotypic Behavior, and Hyperactivity according to ABC subscales. Somnolence and sedation were the most common adverse events, with both events tending to resolve over time.

A unique contribution of this study was the investigation of aripiprazole treatment through an item analysis of the ABC. Significant improvement was observed for those receiving aripiprazole on the following items: "mood changes quickly," "cries inappropriately," and "stamps feet/bangs objects." Although not consistent across treatment arms, additional improvements were observed in tantrum-like items, such as "aggressive toward others," "screams inappropriately," "is irritable," "yells," "demands must be met immediately," "cries over minor hurts," and "has temper outbursts." The most consistent improvement in stereotypic behavior was "repetitive hand, body, or head movement." Numerical improvements were observed on items measuring self-injurious behaviors. However, due to low baseline levels of self-injurious behaviors within the sample, these improvements did not reach statistical significance.

In summary, the state of the research evidence regarding the efficacy, safety, and tolerability of aripiprazole for irritability associated with autistic disorder was sufficient to gain FDA approval in 2009. Even though three randomized controlled trials exist supporting the use of aripiprazole within this population, several limitations can be observed. First, only individuals with a diagnosis of autistic disorder were included within the studies. Therefore, the results

cannot be generalized to youth with other historical pervasive developmental disorders. Second, because of the short duration of each study, long-term benefits and drawbacks cannot be determined. Third, no research exists regarding the benefits of aripiprazole compared to other atypical antipsychotic agents. Lastly, research informing minimally effective or maximally tolerated doses are limited to the findings of Marcus and colleagues (2009), suggesting that the lowest dosage (5 mg/day) was sufficient for significant improvements in irritable behaviors. Additional research in these areas is needed in order to inform psychopharmacological treatment practices.

Antidepressants

Classes of antidepressants that have been studied with individuals with autism spectrum disorder include selective serotonin reuptake inhibitors and tricyclic antidepressants. These agents have primarily targeted repetitive behaviors within this population. Selective serotonin reuptake inhibitors, such as fluvoxamine, fluoxetine, and citalopram, are a class of compounds that are believed to increase the level of the neurotransmitter serotonin by inhibiting its reuptake into the presynaptic cell. Thus, it increases the level of serotonin in the synaptic cleft to bind to the postsynaptic receptor.

Tricyclic antidepressants block the serotonin and norepinephrine transporters in order to elevate synaptic concentrations of these neurotransmitters. Tricyclics have been largely replaced by selective serotonin-reuptake inhibitors or serotonin norepinephrine reuptake inhibitors due to more favorable side effect profiles, but they are still prescribed for certain indications (Stahl, 2008). Randomized controlled trials of fluvoxamine, fluoxetine, and clomipramine have been conducted within populations with autism spectrum disorder (See Table 4.).

Fluvoxamine. Two double-blind placebo-controlled studies have been conducted regarding the efficacy of fluvoxamine, a selective serotonin reuptake inhibitor, in samples of individuals with autistic disorder. The first study conducted by McDougle and colleagues (1996) consisted of 15 adults with autistic disorder. The 12-week study indicated that 53% of participants were categorized as responders according to a rating of "much improved" or "very much improved" on the global improvement item of the CGI. Fluvoxamine proved to be superior to placebo in reducing repetitive thoughts and behaviors, maladaptive behaviors, and aggression, while improving social relatedness and language use. No correlations were found between clinical response and age, autism severity, or IQ. Fluvoxamine was well-tolerated in the treatment group, with mild sedation and gastrointestinal distress being the most notable adverse events.

Sugie and colleagues (2005) added to the research evidence for the efficacy of fluvoxamine by conducting a 12-week randomized, double-blind, placebo-controlled crossover study on a sample of 18 children with autistic disorder. Results of the study indicate that 10 out of 18 of the children responded positively to fluvoxamine according to the Behavioral Assessment Scale (BAS) (Sugiyama, Sugie, Igarashi, Ito, & Fukuda, 1998). Results of the study suggested that 28% exhibited considerable global improvement. A total of 56% showed slight to considerable global improvement, which is similar to the 53% response rate reported by McDougle et al. (1996). The results of these studies suggest that fluvoxamine is safe and efficacious for children and adults with autistic disorder. Considering that only one small randomized controlled trial investigated the short-term safety and tolerability in children with autistic disorder, caution is recommended when prescribing this agent to youth.

Fluoxetine. The efficacy and tolerability of fluoxetine, a serotonin reuptake inhibitor, was evaluated by Buchsbaum and colleagues (2001) in a 16-week, placebo-controlled crossover trial. The study sample included six adult patients with a diagnosis of autistic or Asperger's disorder. Participants in the treatment group displayed significant improvement on the Obsessions subscale of the Yale-Brown Obsessive-Compulsive Scale and the Hamilton Anxiety Scale. Overall, three of the patients improved according to Autism Scores on the Clinical Global Impressions assessment, whereas three patients were unchanged. Significant limitations were evident within the study, including small sample size and lack of systematic monitoring of side effects.

Hollander and colleagues (2005) built on the previous investigation of the effects of fluoxetine on repetitive behaviors in individuals with autism spectrum disorder by examining these effects in a sample of 45 children and adolescents. Participants were randomized into two acute 8-week phases in a double-blind, placebo-controlled crossover study. The primary result of the study indicated that liquid fluoxetine in low doses was more effective at treating repetitive behaviors compared to placebo according to the CY-BOCS with moderate to large effect sizes. Although the findings were insignificant, liquid fluoxetine was also found to be slightly superior to placebo according to the CGI Autism score and a measure of global effectiveness. Lastly, no significant differences were found in the emergence of side effects between treatment and control.

Citalopram. In the sole double-blind, placebo-controlled trial of citalopram that has been conducted, King and colleagues (2009) evaluated the effectiveness of this selective serotonin reuptake inhibitor on a sample of 149 children and adolescents ages 5 to 17 with pervasive developmental disorders. The trial took place across multiple sites. King et al. (2009) concluded

that citalopram was ineffective for the treatment of repetitive behaviors associated with autism spectrum disorder. No significant reductions were found between the treatment and placebo groups according to the CY-BOCS, and no significant differences were found in the rate of positive responses on the Improvement subscale of the CGI. Moreover, use of the agent was significantly more likely to be associated with adverse events, including increased energy level, impulsiveness, decreased concentration, hyperactivity, stereotypy, diarrhea, insomnia, dry skin, or severe itching of the skin.

Clomipramine. Clomipramine hydrochloride is a serotonin reuptake blocker with properties that combat obsessive behaviors (Gordon, State, Nelson, Hamburger, & Rapoport, 1993). Two randomized controlled trials support the efficacy of this agent within populations with autistic disorder. Gordon and colleagues (1993) conducted a 10-week, double-blind, crossover study of clomipramine versus placebo in a sample of 12 subjects aged 6 to 18 years with autistic disorder. Results of the study suggest that clomipramine was superior to placebo at reducing stereotypies, repetitive and ritualistic behavior, and compulsions at doses ranging from 25 to 250 milligrams per day. No statistically significant differences in adverse events were found between the treatment and placebo group. One subject presented with a seizure in the second week of treatment. Other adverse events included insomnia, constipation, twitching, and tremors.

The second randomized controlled trial of clomipramine was completed by Remington, Sloman, Konstantareas, Parker, and Gow (2001) in order to compare the effects of clomipramine and haloperidol on stereotypic behavior in a double-blind, placebo-controlled, crossover study. A sample of 31 subjects under 20 years of age completed a 7-week trial of haloperidol, clomipramine, or placebo. Average doses of clomipramine ranged from 100 to 150 milligrams

per day. Results of the study suggested that haloperidol was more effective than clomipramine at reducing stereotypic behavior. The study results also indicated that no significant differences were observed between the clomipramine and control groups for stereotypies, irritability, or hyperactivity according to the ABC. Twice as many participants in the clomipramine group discontinued the study due to side effects, which included tachycardia, tremors, lethargy, insomnia, diaphoresis, nausea, or lack of efficacy.

Overall, studies of the tricyclic antidepressant, clomipramine, suggest that the agent is ineffective at reducing stereotypies, repetitive and ritualistic behavior, and compulsions for individuals with autistic disorder (Gordon et al., 1993). It was also found to be less effective than haloperidol, with twice as many presenting side effects (Remington et al., 2001). However, research regarding the effect of selective serotonin reuptake inhibitors on repetitive behaviors is mixed. While citalopram was found to be ineffective at decreasing obsessions or fostering global improvement, fluvoxamine was found to be associated with slight to considerable improvement for children with autistic disorder and fluoxetine was found to be lead to significant improvement in repetitive behavior and obsessions in children and adolescents with autistic disorder.

Stimulants

Initial research on the use of stimulants in children to ameliorate inattention and hyperactivity associated with autism found that it was contraindicated, leading to increases in stereotypic movements and irritability (Campbell et al., 1978). However, several methodological issues were present within the research, including heterogeneous samples of children with diverse psychiatric disorders and previous use of neuroleptics without a washout period (Quintana et al., 1995). In response, several small scale uncontrolled studies were completed in order to decipher the effects of stimulants on attention, impulsivity, and hyperactivity of children

with autism spectrum disorder. Results of these studies suggest improvements in attention (Birmaher, Quintana, & Greenhill, 1988; Strayhorn, Rapp, Donina, & Strain, 1988), concentration (Hoshino, Kumashiro, Kanero, & Takahashi, 1977), hyperactivity (Birmaher et al., 1988; Geller, Guttmacher, & Bleeg, 1981; Hoshino et al., 1977), impulsivity (Birmaher et al., 1988; Hoshino et al., 1977), aggression (Geller et al., 1981), destructive behavior, and stereotypic movements (Strayhorn et al., 1988). As a result, rigorous studies were developed to investigate the efficacy of this drug class for youth with autism spectrum disorder (See Table 5.).

Methylphenidate. To improve the state of the evidence regarding the efficacy of stimulant medications in children with autism spectrum disorder, Quintana et al. (1995) conducted the first randomized controlled trial of methylphenidate for this population. A sample of 10 children ages 7 to 11 who had a DSM-III-R diagnosis of autistic disorder participated in a double-blind crossover study. Participants were randomly assigned to placebo, 10 milligrams of methylphenidate, or 20 milligrams of methylphenidate. While results were modest, methylphenidate was associated with statistically significant improvement in hyperactivity over placebo. Additionally, no significant side effects were found in the treatment groups versus placebo. This included no worsening of behavior or increases in stereotypic movements, as was the primary concern within prior research (Campbell et al., 1978).

A second double-blind, placebo-controlled crossover study was conducted by Handen, Johnson, and Lubetsky (2000). Thirteen children ages 5 to 11 were randomly assigned to placebo, 0.3 milligrams per kilogram of methylphenidate, or 0.6 milligrams per kilogram of methylphenidate. Positive responses were operationalized by a 50% increase on the Teacher Conners Hyperactivity Index. Sixty-one percent of participants responded. This finding suggests that methylphenidate is a reasonable treatment option for children with autism who also present

with symptoms of attention-deficit hyperactivity disorder. Significant decreases in stereotypies and inappropriate behavior were also observed. However, no statistically significant differences were found in the core symptoms of autism as determined by the Child Autism Rating Scale.

In contrast to the findings in the Quintana et al. (1995) study, significant side effects were found in the Handen et al. (2000) study. Three children (23%) were unable to complete the trial due to adverse side effects, which included crying, tantrums, aggression, and skin picking. Additional side effects included increases in irritability and social withdrawal. Because sedation cannot easily be discerned from drowsiness, social withdrawal, and lethargy within rating scale outcome measures, the authors state that these variables need to be assessed as potential side effects through additional research. Side effects appeared to be more prevalent in the group receiving a higher dose (0.6 milligrams per kilogram per day). Lastly, the Handen et al. (2000) highlighted that adverse effects present soon after the psychopharmacologic treatment is initiated. This presentation allows for clinicians to immediately assess those who are exhibiting tolerable responses to methylphenidate early within treatment.

Given inconclusive findings regarding the efficacy and tolerability of methylphenidate for children with pervasive developmental disorders and the small samples sizes present within the previous randomized controlled trials, a larger scale study was implicated. RUPP (2005) carried out a double-blind, placebo-controlled, crossover study on a sample of 72 children ages 5 to 14 years with a diagnosis of a pervasive developmental disorder and symptoms of severe hyperactivity. Doses were determined according to weight and were administered in divided doses ranging from 7.5 to 50 milligrams per day. According to the hyperactivity subscale of the ABC, methylphenidate was superior to placebo with small to medium effect sizes ranging from 0.2 to 0.5. Forty-nine percent of children were positive responders to methylphenidate treatment

according to the CGI Improvement rating of "much improved" or "very much improved." In typically developing children with attention-deficit/hyperactivity disorder, response rates range from 70% to 80% (Greenhill et al, 2001).

However, adverse effects were prevalent within the sample, leading to an 18% discontinuation rate. The leading cause of discontinuation was increased irritability. The present magnitude of adverse effects observed was greater than what is observed in children who only hold a diagnosis of attention-deficit/hyperactivity disorder, with results of the MTA study indicating that only 1% of participants experienced adverse events. This study also investigated the effects of potential moderating factors, such as IQ, age, weight, and diagnosis. None of the moderators proved to be significant. Previous research suggests that an IQ of 45 appears to be a threshold for a response to methylphenidate (Aman, Buican, & Arnold, 2003), which is consistent with IQ not presenting as a significant moderator. Also, children with Asperger's and pervasive developmental disorder not otherwise specified were more likely to be labeled as responders to both placebo and methylphenidate than children with Autistic Disorder, although this finding did not reach significance.

Norepinephrine Reuptake Inhibitors

Atomoxetine, a norepinephrine reuptake inhibitor, is typically used as a nonstimulant-based form of attention-deficit/hyperactivity disorder treatment. In the frontal lobe of the brain, norepinephrine transporters also take up dopamine. It is hypothesized that the mechanism of action of atomoxetine is the selective inhibition of the presynaptic norepinephrine transporter, which counteracts behaviors associated with attention-deficit/hyperactivity disorder (Newcorn et al., 2005). Researchers became interested in atomoxetine as a treatment for attention-

deficit/hyperactivity disorder due to length of effect and slow diminution after withdrawal (Arnold et al., 2006).

Atomoxetine. Only one randomized controlled trial has been conducted investigating the efficacy and safety of atomoxetine for children with pervasive developmental disorders with inattention, hyperactivity, and impulsivity as associated features (See Table 6.). Arnold and colleagues (2006) conducted a 6-week randomized placebo-controlled crossover trial on a sample of 16 children ages 5 to 15. Results of the study suggest that atomoxetine is a tolerable and efficacious treatment option for children with autism spectrum disorder. Atomoxetine was found to be significant over placebo according to the Hyperactivity subscale of the ABC. Short-term efficacy was similar to previous trials of methylphenidate and adverse events were less prevalent, with only one participant discontinuing the trial due to increases in aggression. While reductions in hyperactivity were observed, no effects were found for inattentive symptoms often associated with autism spectrum disorder. Due to the absence of additional randomized controlled trials corroborating the findings in this study, further studies of this agent in youth with autism spectrum disorder are necessary in order to further establish the safety and efficacy of atomoxetine.

Alpha-2 Adrenergic Agonists

Clonidine. Two randomized placebo-controlled crossover trials have been conducted regarding the efficacy and tolerability of clonidine for inattention and hyperactivity associated with autism spectrum disorder, which yielded differential results (See Table 6.) (Mohiuddin & Ghaziuddin, 2012). In a double-blind placebo-controlled study of nine males ages 5 to 33, Fankhauser et al. (1992) found that transdermal clonidine led to significant improvement in social relationships and overall behavior, with no significant effect on hyperactivity. A second

study conducted by Jaselskis et al. (1992) found that oral clonidine led to significant improvements compared to placebo in hyperactivity according to the Conners' Abbreviated Parent-Teacher Questionnaire and teacher ratings on the Hyperactivity subscale of the ABC in a randomized, placebo-controlled trial of eight children. Drowsiness and fatigue were common in the treatment phase of both studies compared to placebo group (Fankhauser et al., 1992; Jaselskis et al., 1992). Differential findings and small sample sizes indicate that more research is required in order to determine the efficacy of this agent within populations of youth with autism spectrum disorder.

Anticonvulsants

Anticonvulsants are typically utilized to control seizures, which occur in about 30% of cases of autism. However, the clinical utility of anticonvulsants span beyond seizure control in individuals with autism spectrum disorder. Anticonvulsants are also used in order to treat aggression, mood swings, and hyperactivity, even when a seizure disorder is not present (Mohiuddin & Ghaziuddin, 2012). In the anticonvulsant class of psychotropic medication, research has investigated the efficacy of valproate, lamotrigine, and levitiracetam in youth with autism spectrum disorder (Mohiuddin & Ghaziuddin, 2012). While lamotrigine (Belsito et al., 2001) and levitiracetam (Wasserman et al., 2006) have not been found to be effective, evidence suggests that valproate might have positive effects for this population (See Table 7.) (Anagnostou et al., 2006; Hellings et al., 2005; Hollander et al., 2006, 2010).

Lamotrigine & Levitiracetam. Interest in the pathophysiology of autism spectrum disorder has led researchers to study the effects of lamotrigine, an anticonvulsant agent. A pathophysiological theory was developed due to the intellectual disability and epilepsy that are typically associated with autism spectrum disorder while other skills are preserved. These factors

suggest that the neural mechanisms of autism spectrum disorder are likely to involve early brain development and the modification of synaptic connections (Belsito et al., 2001). Furthermore, postmortem cellular abnormalities have been found in the limbic system and cerebellum individuals with the disorder, areas which enrich glutamate receptors and modulate the excitatory effects of glutamate (Raymond, Bauman, & Kemper, 1996). Increased glutamate activity is essential for typical growth in the second year of life (Kornhuber, Mack-Burkhardt, Konradi, Fritze, & Riderer, 1989) and is vital for synaptic pruning (Belsito et al., 2001). In the case of glutamate overactivity or dysfunction of glutamate receptors, "excitotoxicity" may occur, leading to deviations in normal neural connectivity (Bittigau & Ikonomidou, 1997). As a result, this theory is associated with behavioral characteristics typically manifesting around age two in young children with autistic disorder.

Lamotrigine, an antiepileptic drug, is thought to inhibit voltage-sensitive sodium channels in the brain. This leads to stabilization in neuronal membranes, followed by modulation in presynaptic transmitter release of excitatory amino acids, such as glutamate (Coulter, 1997). The effect of lamotrigine on glutamate led to research interest in looking at lamotrigine as a psychopharmacologic agent in children with autistic disorder. Despite this theory, no significant differences in improvement of autistic features or severity were found between lamotrigine and placebo groups in a study of children ages 3 to 11 in a randomized, double-blind placebo controlled trial (Belsito et al., 2001). A study of another anticonvulsant, levitiracetam, which inhibits presynaptic calcium channels, was not found to have significant effects on behavioral disturbances compared to placebo in a double-blind, placebo-controlled study of 5- to 17-year-olds with autistic disorder (Wasserman et al., 2006).

Valproate & Divalproex Sodium. Valproate, another anticonvulsant, was explored in individuals with autism spectrum disorder due to improvements seen in aggression and self-injury in previous studies of individuals with intellectual disability and other psychiatric disorders with impulsive, compulsive, and neurological features (Hollander et al., 2006). While the mechanism of change of valproate is unknown, animal research suggests that valproate may have anti-aggressive properties and was found to limit the emotional reactivity in mice. Evidence suggests that GABA, an inhibitory neurotransmitter in the brain, may play a role in aggressive behavior (Earley & Leonard, 1977). Other hypotheses have been posed regarding the mechanism of change of valproate, including blocking voltage-gated sodium ion channels, enhancing GABA, inhibiting glutamate, and acting on serotonin and norepinephrine systems (Hollander, Posner & Cherkasky, 2002).

These hypotheses have led to several research studies regarding the effect of anticonvulsants, including valproate and divalproex sodium, on aggression, repetitive behaviors, and irritability in individuals with autism spectrum disorder. However, results of an 8-week, randomized controlled trial of 30 participants indicated that valproate does not lead to significant improvements in aggressive behavior compared to placebo when tested in children and adults with autism spectrum disorder ages 6 to 20. Significant side effects were observed, including increased appetite and skin rash, as well as reports of slurred speech and cognitive slowing (Hellings et al., 2005). In contrast, a 12-week study of 55 children indicated that divalproex sodium had significant effects on irritability when compared to placebo (Hollander et al., 2010). Additionally, a small randomized controlled study of divalproex sodium found favorable results, with the agent leading to significant improvements in repetitive behaviors in a study of 13 individuals with autism spectrum disorder (Hollander et al., 2006).

In summary, the results of the aforementioned research indicate that anticonvulsants have been found to be largely ineffective at improving behaviors associated with autism spectrum disorder. Lamotrigine was found to be ineffective at creating improvements in autistic features (Belsito et al., 2001) and levitiracetam was ineffective at decreasing behavioral disturbances (Wasserman et al., 2006) in youth with autistic disorder. Further, the anticonvulsant, valproate, did not lead to significant improvements in aggression for children and adolescents with pervasive developmental disorders. While Hollander and colleagues (2006) suggest that anticonvulsants may be effective at reducing repetitive behaviors within this population, the aforementioned research evidence including larger sample sizes is sufficient to conclude that anticonvulsants are not an effective treatment for behaviors associated with autism spectrum disorder.

Prevalence of Psychotropic Medications

As highlighted within the previous section, psychopharmacological research has blossomed in the past decade for youth with autism spectrum disorder. Evidence regarding the efficacy of psychotropic agents within this population has led to increased research interest in the prevalence of psychopharmacological agents being prescribed within comprehensive treatment plans for individuals with autism spectrum disorder. The research literature suggests that psychotropic prescribing is prevalent among children and adolescents with autism spectrum disorder and prevalence appears to be increasing.

The first study prevalence study occurred in 1995, which reported that approximately 39% of individuals with autistic disorder were taking either psychotropic or antiepileptic drugs for associated behavioral and psychiatric problems (Aman, Van Bourgondien, Wolford, & Sarphare, 1995). Over time, prevalence of psychotropic medication further increased, with

studies suggesting rates as high as 46% (Aman, Lam, & Collier-Crespin, 2003; Langworthy-Lam, Aman, & Van Bourgondien, 2002) and 56% (Mandell et al., 2008). Although a large proportion of children with autism spectrum disorder receive comorbid diagnoses, a recent study suggested that percentages reach 39% for children with no other diagnoses (Mandell et al., 2008).

The first scientific survey of the prevalence of psychotropic medications to treat behaviors associated with autism spectrum disorder was conducted by Aman and colleagues (1995). This study surveyed 1,595 caregivers of individuals with autism ages 1 to 82 years, with a mean age of 15 years. All participants were members of the Autism Society of North Carolina. Eighty-two percent of the sample was male. Various levels of severity of autism, intellectual disability, and parental education were present and well-distributed within the sample. In addition, approximately 19% of the sample had epilepsy. As a result, the characteristics of the sample were representative of the wide variability of characteristics that are associated with autism spectrum disorder.

The Aman et al. (1995) study received a 53% response rate, with responses from 838 care providers. Psychotropic medication appeared to be heavily used in patients with autism spectrum disorder. Neuroleptics (12%) were the most frequently prescribed psychotropic medications, followed by psychostimulants (7%), anxiolytics (6%), antidepressants (6%) antihypertensives (4%), and mood stabilizers (4%). Caregiver satisfaction ratings suggested that anticonvulsants, antidepressants, and stimulants were rated as the most satisfying psychotropic agents (Aman et al., 1995).

A second survey study conducted by Langworthy-Lam, Aman, and Van Bourgondien (2002) was designed to investigate prevalence and patterns of use of psychotropic and

antiepileptic agents in a sample of individuals with autism spectrum disorder. A survey was mailed to 3,228 families that were members of the Autism Society of North Carolina. The survey received a 48% response rate and a sample size of 1,538 families. The age range of participants ranged from 3 to 56, with a mean age of 15 years of age. Antidepressants were the most frequently prescribed drugs, which were taken by 22% of participants. This differs from findings within the previous study, which only reported 6% of participants being prescribed antidepressants (Aman et al., 1995). Other commonly used psychotropic agents in the current study were antipsychotics (17%), stimulants (14%), anticonvulsants (12%), antihypertensives (10%), sedatives (7%), and mood stabilizers (5%). Within the antipsychotic class, atypical antipsychotics made up approximately 85% of the category. Satisfaction ratings did not significantly differ across medication classes.

A noteworthy contribution of this study was the examination of the relationship between severity of autistic characteristics and psychotropic drug use. More severe autism predicted increased use of any psychotropic medication. Participants with mild or moderate autism were only about 36% as likely to be taking antipsychotics as subjects with severe autism
This relationship was also observed for individual psychotropic agents. Less severe autism predicted the use of stimulant medications, whereas more severe autism predicted the use of antipsychotics (Langworthy-Lam et al., 2002). A later study provided additional support for this relationship (Aman et al., 2003).

The third study also employed survey methodology to examine prevalence rates of psychotropic agents among individuals with autism spectrum disorder (Aman, Lam, & Collier-Crespin, 2003). Seven hundred forty-seven families who were members of the Autism Society of Ohio were surveyed, yielding a 56% response rate. Subject age ranged from 2 to 46 years. While

preschoolers were included within the age range of the survey, prescribing practices within this population did not receive comment. The most common psychotropic agents mirrored the findings from the previous study (Langworthy-Lam et al., 2002), with antidepressants (22%) and antipsychotics (15%) being the most frequently prescribed. Other agents prescribed included antihypertensives (13%), anticonvulsants (12%), stimulants (11%), and mood stabilizers (5%) (See Table 8. for most common individual agents within each medication class). Risperidone accounted for 69% of antipsychotic prescriptions within this study. Average satisfaction ratings suggested that caregivers were similarly satisfied across medication classes (See Table 9.).

Mandell et al. (2008) provided additional data about psychotropic medication use among children with autism spectrum disorder through a cross-sectional study of children enrolled in Medicaid for the 2001 calendar year. It was the first study to investigate psychotropic prescribing patterns exclusively in children and adolescents. The study included 60,641 low-income children from birth to age 21. Neuroleptic drugs were most common within the sample, with 31% of children in the sample being prescribed this medication. The next most prevalent medications were antidepressants (25%), stimulants (22%), mood stabilizers (21%), anxiolytic drugs (12%), and sedatives (3%). Interestingly, children with Asperger's disorder or pervasive developmental disorder were more likely to be prescribed psychotropic medications than children with a diagnosis of autistic disorder, with prevalence rates of 61% and 53%, respectively. This study was the first to include all historical pervasive developmental disorders within the analysis.

The Mandell et al. (2008) study was also the first study to look at prescribing practices within early childhood. The results were striking, indicating that psychotropic prescribing was prevalent during this developmental period. Thirty-two percent of preschool children ages three to five were being prescribed psychotropic agents. Neurolpetics and stimulants were the most

frequently prescribed. Children ages zero to two had a prescribing rate of 18%, with sedatives being the most commonly prescribed agent. The state of the research has not readily explored use of psychotropic agents within this age range. No randomized controlled trials have been conducted with young children. This suggests that prescribing practices are preceding an evidence-base for use within early childhood populations. Moreover, these percentages are significantly higher than psychotropic prevalence rates among Medicaid-eligible children in general, with a prevalence rate of one percent being reported for children ages two to four years within previous research (Zito, Safer, dosReis, Gardner, Boles, & Lynch, 2000). A study of Medicaid-enrolled children in general reported a prevalence rate of 10%, which is approximately five times less than was reported for children with autism spectrum disorder (Zito, Safer, Zuckerman, Gardner, & Soeken, 2005).

While several studies have examined psychotropic prevalence rates, the first three studies were conducted through survey-methodology and self-report. Subjects were drawn from the Autism Society of various states, which may not be representative of the population of individuals with autism spectrum disorder in general. Although the most recent, largest scale, nationally representative study was published in 2008, the sample included claims from the 2001 calendar year. Since that time, two atypical antipsychotics were FDA approved, highlighting the validated use of psychotropic medications for young children with autism spectrum disorder. Despite this fact, increases were already observed within research between 1995 and 2003. As a result, it can be hypothesized that further increases could be observed since that time. However, this has not yet been investigated within the literature (See Figure 2)

Of the four aforementioned prevalence studies, only one study examined psychotropic prevalence rates exclusively among preschoolers, children, and adolescents (Mandell et al.,

2008). The Mandell et al. (2008) was also the only study to stratify across pervasive developmental disorders and provide insight regarding how diagnosis might affect the prescribing practices of clinicians. Given these facts, further investigation of psychotropic prevalence rates among youth with autism spectrum disorder is warranted.

Other research groups have investigated prevalence using subsets of the population with autism spectrum disorder. First, Martin, Scahill, Klin, and Volkmar (1999) intended to build upon the original findings of Aman and colleagues (1995) by investigating rates and patterns of psychotropic drug use among higher-functioning children with a diagnosis of Asperger's, autistic disorder, or pervasive developmental disorder not otherwise specified. Higher-functioning status was operationalized by an IQ greater than or equal to 70. The sample consisted of 109 families seeking enrollment in the Yale Child Study Center's Project on Social Learning Disabilities. Of the 109 subjects, 55% were taking psychotropic medications. Approximately 70% of participants had taken a psychotropic medication at some point in their lives, indicating that pharmacotherapy is a common treatment for higher-functioning individuals with autism.

The most frequently prescribed medication among higher-functioning individuals with autism was antidepressants, which was prescribed for 32% of participants. Stimulants (20%) and neuroleptics (17%) were the next most frequent prescriptions. This finding differed from the previous research suggesting that neuroleptics were most frequently prescribed within a sample of individuals with a wide distribution of IQ scores (Aman et al., 1995). The most frequent specific agent found was selective serotonin reuptake inhibitors. However, high-functioning children with social disabilities are often initially diagnosed with attention-deficit/hyperactivity disorder due to the lessened severity of autistic characteristics. Further, it has been hypothesized

that attention-deficit /hyperactivity disorder may be a discrete comorbid diagnosis for high-functioning children with autism spectrum disorder.

An additional contribution to the literature provided by the Martin et al. (1999) study included investigations of the association between psychotropic medications and presenting symptom clusters. Atypical neuroleptics were associated with aggression, self-injurious behaviors, and obsessive-compulsive symptoms. Antidepressants were also associated with obsessive-compulsive and ritualistic behaviors, as well depression and anxiety. The use of stimulants were directly associated with inattention and distractibility. Antihypertensives were associated with anxiety symptoms. However, no symptom patterns were associated with the use of anxiolytic, mood stabilizer, or traditional neuroleptic medications.

A research study conducted by Sullivan and Sadeh (2015) analyzed psychotropic prevalence within another subset of the population, adolescents with autism spectrum disorder. In a broader study of adolescents across disabilities, 43% of adolescents with autism spectrum disorder diagnoses were found to be prescribed any psychotropic drug. Further, 24% of adolescents with this disorder were prescribed polypharmacy intervention, and 23% were prescribed more than one class of psychotropic medication. Antidepressants (23%), antipsychotics (18%), and stimulants (14%) were the most frequently prescribed agents for adolescents with autism spectrum disorder. Analyses of subsets of this population provide important additions to the research literature and inform how psychotropic prescribing differs for youth across the autism spectrum during the developmental progression.

Prevalence of Polypharmacy

When researchers began studying psychopharmacological treatment practices for youth with autism spectrum disorder, approximately 22% of individuals were taking one psychotropic

drug, 6% were taking two, 2% were taking three, and less than 1% were taking four (Aman et al., 1995), leading to a total of 9% of children taking two or more medications. Eight years later, 21% of individuals with autistic disorder were taking two or more psychotropic drugs, which is more than double of what was previously reported (Aman et al., 2003). Children with Asperger's disorder and high functioning children with autistic disorder were found to have even higher rates of polypharmacy, with 53% taking two or more drugs simultaneously. It has also been reported that 20% of low-income children with autism spectrum disorder were prescribed more than three medications concurrently over the course of one year (Mandell et al., 2008). Statistics regarding the increasing rates of polypharmacy are dramatic. The current literature is devoid of research regarding the utilization of multiple psychotropic agents within developing children; therefore, caution is warranted when considering the utilization of several simultaneous psychotropic agents.

Predictors of Psychopharmacological Treatment for Autism Spectrum Disorder

Evidence within the research literature regarding general psychopharmacology practices and psychopharmacological practices for individuals with autism spectrum disorder suggests that individual characteristics, such as age, gender, race/ethnicity, and comorbid diagnoses, as well as county-level characteristics, may affect prescribing practices for youth with autism spectrum disorder. As a result, variables beyond the scope of medical best practice may be influential within psychopharmacological treatment for youth with autism spectrum disorder.

Age. Patient age has been found to be a powerful predictor of the use of any psychotropic drug for individuals with autism spectrum disorder. Greater age predicted the use of any psychotropic medication (Aman et al., 1995; Aman et al., 2003; Langworthy-Lam et al., 2002; Mandell et al., 2008) and use of individual psychotropic agents, including antipsychotics (Aman

et al., 1995; Langworthy-Lam et al., 2002), antidepressants, mood stabilizers, and sedatives (Langworthy-Lam et al., 2002). In contrast, younger age predicted the use of stimulant medication (Langworthy-Lam et al., 2002). With each year of age, Langworthy and colleagues (2002) suggested that the likelihood of being prescribed some form of medication increases by approximately 3% for individuals with autism spectrum disorder. The findings within the Martin et al. (1999) study regarding the effect of age on prescribing practices were commensurate with previous findings, indicating that the use of any medication also increases with age in individuals with Asperger's or high functioning autism. The relationship between age and use of psychotropic medications among youth with autism spectrum disorder is consistent across research studies (Martin et al., 2003).

Several hypotheses have been posited regarding age-related effects on psychotropic prevalence rates. This finding may be due to the emergence of comorbid disorders later in life, such as anxiety and depression. Additionally, increases in weight and size occur as children age, particularly during puberty, which may increase the need for psychotropic medications that prevent irritability, aggression, hyperactivity, and self-injury in order to prevent harming themselves or others (Langworthy-Lam & Van Bourgondien, 2002).

While age-related trends have been documented within psychotropic prescribing, only one study exclusively examined children and adolescents with autism spectrum disorder. The same study was the only examination of the occurrence of psychotropic drugs within early childhood, with results suggesting that psychotropic medications are prevalent within this subset of the population (Mandell et al., 2008). The onset of autism spectrum disorder occurs prior to three years of age, with most prominent manifestations being able to be observed after age 2 (American Psychiatric Association, 2000). Research outside of the realm of autism spectrum

disorder indicates that sizeable increases in prescription rates have been seen within the general population (Zito, Safer, dosReis, Gardner, Boles, & Lynch, 2000). Given the early identification of the disorder and general increases in psychotropic prevalence rates within preschool populations, it can be hypothesized that psychotropic prevalence rates are also increasing for young children with autism spectrum disorder.

Gender. The research regarding the effect of gender on psychotropic prescribing within youth with autism spectrum disorder has produced mixed results. In the first prevalence study, no specific medication class was significantly associated with gender (Aman et al., 1995). The previous research finding notwithstanding, other findings indicate that low-income males with autism spectrum disorder were more likely to have received psychotropic medications than females (Mandell et al., 2008). In a sample of individuals with Asperger's and high functioning autism, females were more likely to be prescribed antidepressants and anticonvulsants than males (Martin et al., 1999). Overall, the effect of gender on psychopharmacological practices within this population is inconclusive. However, in a study of general psychopharmacology among youth, males were found to be more likely to receive psychotropic medications (Martin, Van Hoof, Stubbe, Sherwin, & Scahill, 2003) when compared to females.

Lack of overall gender-related effects may be attributable to small percentages of females within prior prevalence studies (Aman et al. (1995): 18%; Martin et al. (1999): 17%; Langworthy et al. (2002): 18%, Aman et al. (2003): 18%; Mandell et al. (2008): 22%) for this population. The gender distribution within the studies is consistent with the gender-related features of autism spectrum disorder, with rates being four to five times higher in males than in females (American Psychiatric Association, 2000). Females with autistic disorder are more likely than males to exhibit severe intellectual disability. As will be subsequently discussed, individuals with autism

spectrum disorder who also present with moderate or severe intellectual disability have an increased likelihood of being prescribed psychotropic medications (Aman et al., 2003; Langworthy-Lam et al., 2002). In conclusion, gender-related features of the disorder may affect psychopharmacological prescribing practices. However, the current state of the research regarding gender-related effects yielded mixed results.

Race/Ethnicity. It is a general acknowledgement among the scientific community that autism spectrum disorder occurs equitably across demographic groups (Dyches, Wilder, Sudweeks, Obiakor, & Algozzine, 2004). In spite of this acknowledgement, research suggests that race and ethnicity lead to disparities in diagnosis and access to care for children with autism spectrum disorder. Research has suggested that White children are more likely to receive psychotropic medications, whereas Asian children are less likely. Specifically, according to Mandell and colleagues (2008), 61% of White children were receiving psychotropic medications, whereas only 43% of Asian children were receiving psychotropic medications. In another study of predictors of use of individual psychotropic agents, being White was significantly associated with being prescribed antidepressants compared to other ethnicities (Langworthy et al., 2002).

Similar racial disparities were observed within the general psychotropic prevalence rates reported by Zito et al. (1998), with African American youth being less than half as likely to receive psychopharmacological treatments when compared to White children ages 5 to 14. Even when controlling for geographic variation, the aforementioned racial disparities persisted. An additional analysis indicated that children receiving psychotropic medications were less likely to be African American or Hispanic (Martin et al., 2003). Furthermore, Hahn (1995) found that Black and Hispanic children were less likely to receive prescription medications when compared to their White counterparts. The findings remained even when controlling for health conditions,

number of physician visits, and socioeconomic status, highlighting ethnic minorities as an underserved population. Lastly, an examination of prescription drug expenditures within the Georgia Medicaid population indicated that Black children were found to receive approximately three fewer prescriptions than White children (Khandker & Simoni-Wastila, 1998).

Investigating racial and ethnic influences on psychotropic prescription rates is a complex issue. Differences in reported medication utilization may be influenced by the ability for racial and ethnic groups to access services. Liptak and colleagues (2008) indicated that being Black or Latino was associated with decreased access to services for children with autism spectrum disorder (Liptak et al., 2008). Decreased access to services may lead to under identification of children from various demographic groups within early childhood (Norbury & Sparks, 2013). African American children are diagnosed 18 months later than White children, on average (Mandell, Listerud, Levy, & Pinto-Martin, 2002). These diagnoses were also more likely to change over time (Mandell, Ittenbach, Levy, & Pinto-Martin, 2007). Taken together, these facts suggest that minorities appear to be medically underserved, leaving them less likely to receive psychotropic medications for the treatment of the behaviors associated with autism spectrum disorder.

Differences in observed psychotropic medications can be influenced by the attitudes and belief systems that influence use of mental health services for ethnic minorities. Black children have been found to have higher levels of mistrust and negative attitudes associated with use of professional mental health services compared to White children. For instance, mental health services can be viewed as a culturally inconsistent way of addressing life problems for ethnic minority groups, and accessing mental health care can be perceived as socially stigmatizing (Matthews & Hughes, 2001).

Furthermore, racial and ethnic differences in psychotropic medication utilization span beyond difference in identification, access, and pursuit of care. Prior research has suggested that Black individuals express less willingness to use psychiatric medications themselves or to administer them to a child within his or her care. These findings have been found to persist beyond individual characteristics, including knowledge, socioeconomic status, and religious affiliation. Researchers suggest that the reluctance surrounds the beliefs about the efficacy and side effects of psychotropic medications within this population (Schnittker, 2003).

Comorbid Diagnoses. It is common for children with autism spectrum disorder to have comorbid diagnoses. When children with autism spectrum disorder have a comorbid diagnosis, they are more likely to be prescribed psychotropic drugs and to receive polypharmacy intervention. For example, comorbid intellectual disability is common in children with autism spectrum disorder, which has been found to predict greater use of psychotropic agents (Aman et al., 1995; Aman et al., 2003; Langworthy et al., 2002). In a national study of service and treatment utilization, children with autism spectrum disorder who had a comorbid intellectual disability were found to be significantly more likely to receive psychotropic medication (Zablotsky et al., 2015). In addition, psychotropic medications are more common among those with moderate or severe intellectual disability and less common among children with mild intellectual disability (Mandell et al., 2008). It has also been suggested that individuals with moderate to profound retardation were about five times more likely to receive antiepileptic medication when compared to individuals with mild or no intellectual disability (Aman et al., 1995), whereas less severe intellectual disability predicted the use of stimulant medication (Langworthy-Lam et al., 2002).

Age-related and developmental differences are important considerations when thinking about comorbid diagnoses and pharmacotherapy among individuals with autism spectrum disorder. For instance, hyperactivity may warrant stimulant medications earlier in life, when the highest levels of activity and impulsivity are present (Martin et al., 1999). According to a study of attention-deficit/hyperactivity disorder in the context of autism spectrum disorder, between 28% and 78% of children with autism spectrum disorder meet the diagnostic criteria for the attention-deficit/hyperactivity disorder (Murray, 2010). The DSM-IV-TR did not allow for the comorbid coding of both diagnoses (American Psychiatric Association, 2000). However, this frequently occurred within clinical practice (Kaplan & McCracken, 2012). It has been recognized that children who meet both sets of diagnostic criteria have more severe clinical difficulties than children with an autism spectrum disorder diagnosis alone (Gadow, DeVincent, & Pomeroy, 2006).

Depression is especially common in adolescence and adult life for those individuals with autism spectrum disorder who have the intellectual capacity to recognize their level of impairment (American Psychiatric Association, 2000). Comorbid anxiety and depression are also more prevalent in individuals of greater age and higher IQ (Mayes et al., 2011). The later presentation of comorbid diagnoses may serve to explain trends within psychopharmacological research within this population, which suggests increasing prevalence in psychotropic drug use as children age (Aman et al., 1995; Aman et al., 2003; Langworthy-Lam et al., 2002; Mandell et al., 2008).

It has been established that comorbid diagnoses, such as intellectual disability, attention-deficit/hyperactivity disorder, depression, and anxiety, commonly occur in youth with autism spectrum disorder. This fact, in combination with the observed influence of comorbid diagnoses

on psychopharmacological practices, suggests that the presence of a comorbid diagnosis plays an important role during provision of psychopharmacological intervention. Despite this observed relationship, a recent study of parental perceptions suggested that despite the high prevalence of utilization of behavioral health services and psychotropic prescriptions for youth with autism spectrum disorder, 30% of parents reported feeling as though their child's developmental needs were still not being met (Zablotsky et al., 2015). This finding highlights the complex behavioral health needs for youth with autism spectrum disorder, especially in the presence of psychiatric comorbidities.

County Demographics. According to the Autism Society of America (2000), the occurrence of autism is equitable across levels of family income and educational levels. Nevertheless, socioeconomic status has been found to be influential within the assessment and treatment of youth with autism spectrum disorder. For example, economically disadvantaged communities tend to be associated with lower rates of autism identification (16 per 10,000) and decreased access to healthcare services (Liptak et al., 2008). Access and utilization of healthcare services are pertinent for the early identification and assessment of autism spectrum disorder, as well as for the provision of behavioral and psychopharmacological interventions for the treatment of the behaviors associated with autism spectrum disorder.

Effects of poverty on psychopharmacological treatment of this population have been observed. A study of youth with autism spectrum disorder within a Medicaid population, a program designed to provide medical and health-related services for families with low levels of income and resources, produced the highest level of psychotropic prescription rates among the prevalence studies (Mandell et al., 2008). However, another study suggested that higher levels of parental education have been found to predict greater psychotropic medication utilization for

children with autism spectrum disorder (Langworthy-Lam et al., 2002), with level of parental education being one variable considered in the conceptualization of poverty. Given the inconclusive nature of these findings, the effect of low socioeconomic status on psychopharmacological prescribing practices warrants further consideration.

Additional county demographic characteristics have been found to serve as predictors of psychopharmacological treatment for youth with autism spectrum disorder. For instance, children with autism spectrum disorder living in predominantly urban counties have been found to be less likely to be treated with psychotropic medications than those in less urban counties, whereas children with autism spectrum disorder living in counties with greater proportions of White residents have been found to be more likely to receive psychopharmacological intervention (Mandell et al., 2008).

Furthermore, county education characteristics have been shown to influence autism identification and treatment practices. In a study regarding county-level variation in the prevalence of Medicaid-enrolled youth with autism spectrum disorder, counties with lower student expenditures, a higher number of per capita number of pediatricians and pediatric specialists, a greater number of Medicaid-enrolled youth, and a greater percentage of White residents had higher prevalence of youth with autism spectrum disorder. Counties in which there was a greater proportion of students receiving special education services was also associated with a greater number of Medicaid-enrolled children, which may positively influence access to healthcare (Mandell et al., 2010). As such, county educational characteristics may influence access to medical and behavioral health care for youth with autism spectrum disorder. As a result, educational characteristics may play an influential role in whether or not youth are

prescribed psychopharmacological intervention for behaviors associated with autism spectrum disorder.

In summary, individual child and adolescent characteristics, as well as county demographic, healthcare, and educational characteristics, have been identified as variables that affect the identification and healthcare utilization for youth with autism spectrum disorder. As a result, these variables may have influential effects on the presence or absence of psychopharmacological intervention for youth with autism spectrum disorder. The effect of these variables on psychopharmacological prescribing practices for this population will be examined within the current study.

Use of Medicaid Claims for Psychopharmacological Research

Medicaid is a joint venture between the federal government and the states to provide medical and health-related services for families with limited resources. The federal government developed minimum guidelines for service provision, but the states have the latitude to expand the type, amount, duration, and scope of services beyond the established guidelines. Children enrolled in Medicaid are entitled to a comprehensive set of health care services. Medicaid-enrolled children and families utilize these services at a much higher rate than those that are uninsured (www.medicaid.gov).

Medicaid was enacted through amendments to the Social Security Act in 1965. Federal guidelines mandate that qualified parents, children, pregnant women with low income, older adults with disabilities, and people with disabilities and low-income are eligible for services. The state of Michigan determines eligibility for Medicaid in relation to a specified percentage of the federal poverty line.

Utilizing a Medicaid-enrolled population for research related to psychotropic treatment is advantageous because Medicaid has less restrictive formulary and copayments than private insurance, minimizing the barriers to health-related services (Safer, Zito, & Gardner, 2004). Having a Medicaid or State Children's Health Insurance program has also been found to be associated with better access to health services for children with autism spectrum disorder across racial and ethnic groups (Liptak et al., 2008). Children with autism spectrum disorder are also disproportionately eligible for Medicaid due to the nature of the disability, indicating an additional benefit of utilizing a Medicaid-enrolled sample to examine treatment practices. As a result, utilization of Medicaid insurance claims to evaluate treatment practices in common within previous psychopharmacological research.

Present Study

The purpose of this study was to contribute to the literature on the prevalence of psychotropic medications for youth with autism spectrum disorder within a diverse sample of Medicaid-enrolled children and adolescents in the state of Michigan in the year 2009. No previous studies have investigated psychopharmacological prevalence rates in the state of Michigan. Prevalence of psychopharmacological treatment and rates of polypharmacy were analyzed. The predictive value of participant- and county-level variables, including demographic, healthcare, and educational characteristics, on psychopharmacological prescribing practices were analyzed. Lastly, change over time in psychopharmacological prevalence rates and rates of polypharmacy intervention between 2001 and 2009 were analyzed due to the substantial research conducted regarding the efficacy of psychopharmacological intervention that occurred during that time period for individuals with autism spectrum disorder. Results of the study have implications for clinical practice and provide updated information regarding

psychopharmacological prevalence rates for youth with autism spectrum disorder. Furthermore, results of the study allow for the identification of variables beyond the scope of medical best practice that are influential within psychopharmacological prescribing, which may allow for targeted service outreach to underserved populations of youth with autism spectrum disorder.

Research Questions

1) What was the prevalence of psychopharmacological treatments for Medicaid-enrolled youth with autism spectrum disorder during the 2009 calendar year in Michigan?

Previous studies of psychopharmacological prescribing for individuals with autism spectrum disorder indicate prevalence rates ranging from 39% to 56%, with apparent increases in prevalence rates between 1995 and 2003 (Aman et al., 1995; Mandell et al., 2008). Only one study focused exclusively on children and adolescents and low socioeconomic status (Mandell et al., 2008). Drawing on the findings from the study with greatest generalizability to a sample of low-income children in Michigan (Mandell et al., 2008), as well as observations of rising psychopharmacological prevalence rates within this population and childhood populations in general, it was hypothesized that the prevalence rate of psychopharmacological prescriptions use will be exceed previously identified prevalence rates (i.e., 39-56%) (Mandell et al., 2008). The null hypothesis was that similar rates of psychopharmacological prevalence (i.e., 39-56%) would be observed within the current study.

2) How many Medicaid-enrolled youth (ages 0-17) with autism spectrum disorder in Michigan were utilizing more than one concurrent psychotropic medication during the 2009 calendar year?

In 1995, approximately 9% of children with autism spectrum disorder were taking more than one concurrent psychopharmacological medication. In 2001 (Mandell et al., 2008) and 2003 (Aman

et al., 2003), rates of polypharmacy rose to approximately 20%. It was hypothesized that rates of polypharmacy within Michigan would be greater than or equal to 20% for children with autism spectrum disorder within the current study. The null hypothesis stated that similar rates of polypharmacy intervention (i.e., 20%) would be observed within the current study.

3) Does age group (Age Group 1: 0-5, Age Group 2: 6-12, Age Group 3: 13-17) serve as a significant predictor of psychopharmacological prescribing practices for Medicaid-enrolled youth with autism spectrum disorder during the 2009 calendar year when controlling for other independent variables?

Only one previous study examined prescribing practices within the early childhood period for children with autism spectrum disorder (Mandell et al., 2008). Findings indicated that 18% of children between zero and two and 32% of children between three and five were being prescribed psychotropic agents. In contrast, prevalence studies examining a broader age range from childhood to adulthood yielded prevalence rates of 39% (Aman et al., 1995) and 56% (Mandell et al., 2008). It was hypothesized that older age will be associated with greater use of psychopharmacological intervention, as is suggested within the research literature (Aman et al., 1995; Aman et al., 2003; Langworthy-Lam et al., 2002; Mandell et al., 2008).

4) Does historical pervasive developmental disorder diagnosis (i.e., autistic disorder, Asperger's disorder, pervasive developmental disorder not otherwise specified) significantly predict psychopharmacological prescribing practices for youth living in Michigan in the year 2009 when controlling for other independent variables (i.e., age, gender, race/ethnicity, presence of comorbid diagnosis, county demographic/healthcare/education characteristics)?

Fifty-five percent of high-functioning children with autism spectrum disorder were taking psychotropic medications according to a previous study, with 70% of the sample indicating that they had taken a psychotropic medication at one point in their lives (Martin et al., 1999). This percentage exceeds prevalence rates for general populations of children with autistic disorder or across pervasive developmental disorders, which range from 39% to 56% (Aman et al., 1995; Mandell et al., 2008). Rates of polypharmacy within high-functioning autistic populations have also been found to exceed that of overall populations of individuals with autism spectrum disorder, with rates of 53% (Martin et al., 1999) and 20%, respectively. Therefore, it was hypothesized that psychopharmacological prescribing would be more prevalent for youth with Asperger's disorder than youth with autistic disorder. The null hypothesis suggests that type of pervasive developmental disorder does not have a significant effect on psychopharmacological prescribing practices.

5) Does the presence of comorbid diagnoses (e.g., intellectual disability, attention-deficit/hyperactivity disorder, depression, and anxiety) significantly predict psychopharmacological prescribing for Medicaid-enrolled youth with autism spectrum disorder in Michigan in 2009 when controlling for other independent variables (i.e., age, gender, race/ethnicity, presence of comorbid diagnosis, county demographic/healthcare/education characteristics)?

It has been suggested that children with autism spectrum disorder who have a comorbid diagnosis are more likely to be prescribed psychotropic drugs and to receive polypharmacy intervention (Aman et al., 1995; Aman et al., 2003; Langworthy et al., 2002). The strongest findings have surrounded comorbid intellectual disability, which is present in the majority of children with autistic disorder and predicts greater use of psychotropic agents (Aman et al., 1995;

Aman et al., 2003; Langworthy et al., 2002 Mandell et al., 2008, Martin et al., 1999). As a result, it was predicted that youth with a comorbid diagnosis will experience greater levels of psychopharmacological prescribing than youth without a comorbid diagnosis. The null hypothesis suggests that the presence of a comorbid diagnosis does not have a significant effect on psychopharmacological prescribing, with the study yielding similar prescribing practices for youth with and without comorbid diagnoses.

6) Do demographic characteristics, including gender, race/ethnicity, and county characteristics (e.g., demographic, healthcare, education) serve as significant predictors of psychotropic medication utilization among Medicaid-enrolled children (ages 0-17) in Michigan in 2009?

Predictors of greater levels of psychopharmacological prescribing have been suggested within the literature regarding the treatment of autism spectrum disorder. Predictors include greater age (Aman et al., 1995; Aman et al., 2003; Langworthy-Lam et al., 2002; Mandell et al., 2008) and being Caucasian (Hahn, 1995; Mandell et al., 2008; Martin et al., 2003; Zito et al., 1998). In addition, county-level variables, including low socioeconomic status (Mandell et al., 2008), greater number of White residents (Mandell et al., 2008), and greater proportion of students in special education, have also been associated with differences in health care utilization and access to psychopharmacological intervention. Therefore, it was hypothesized that these variables will serve as significant predictors of psychopharmacological prescribing within youth with autism spectrum disorder in the state of Michigan. The null hypothesis suggests that demographic variables do not have a significant effect on psychopharmacological treatment practices.

7) Did the prevalence of psychotropic prescribing significantly increase among Medicaid-enrolled youth (ages 0-17) with autism spectrum disorder between 2001 and 2009 in Michigan?

Based on the findings of previous prevalence studies, it appears that psychopharmacological prescribing practices for autism spectrum disorder increased from 39% in 1995 (Aman et al., 1995) to 56% in 2003 (Mandell et al., 2008). This finding, in addition to increasing trends in general psychopharmacological prescribing within youth populations regardless of diagnosis (Zito, Safer, dosReis, Gardner, Boles, & Lynch, 2000) and recent FDA approval of two psychopharmacological medications that treat the irritability associated with autism spectrum disorder, leads to the hypothesis that greater levels of psychopharmacological prescribing in Michigan Medicaid samples were observed in the year 2009 when compared to 2001. The null hypothesis states that no significant change in psychopharmacological prevalence can be observed over time.

Chapter 3:

Methods

The purpose of this study was to examine the prevalence of psychotropic medications for children and adolescents with autism spectrum disorder within a sample of Medicaid-enrolled youth in the state of Michigan. Prevalence of psychopharmacological treatment and rates of polypharmacy were analyzed using insurance claims from the 2009 calendar year. The effects of individual characteristics, such as age, gender, race/ethnicity, autism spectrum disorder diagnosis, and presence of psychiatric comorbidities, on psychopharmacological prescribing practices were analyzed. The effects of county-level variables, such as demographic, healthcare, and educational characteristics, on psychopharmacological prescribing were also investigated. In addition, the study examined differences in psychopharmacological prescribing practices in 2001 and 2009 in the context of advances made within psychopharmacological research over this time period for youth with autism spectrum disorder.

Participants

Subjects were considered to have an autism spectrum disorder diagnosis if they had at least one health care utilization claim and a listed diagnosis of autistic disorder (299.0), Asperger's disorder (299.8), or unspecified pervasive developmental disorder (299.9) according to the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) (National Center for Health Statistics, 2002). The following descriptive statistics are presented according to participant characteristics in the 2001 and 2009 data sets.

Of the 4,753 subjects within the 2001 sample, 4,003 (84%) participants had a diagnosis of autistic disorder, 742 (16%) participants had a diagnosis of Asperger's Disorder, and 8 (0.2%) participants had a diagnosis of an unspecified pervasive developmental disorder. With regards to

comorbid diagnosis, 3,007 (63%) participants were identified as having at least one comorbid psychiatric diagnosis. The most common comorbid diagnoses were communication and developmental disorders (56%), intellectual disability (9%), attention-deficit/hyperactivity disorder (4%), mood disorders (2%, and disruptive behavior disorders (2%). All other comorbid diagnoses accounted for less than 1% of the sample.

The majority of subjects (59%) ranged from 6 to 12 years of age (N = 2,824). One thousand six hundred twenty-eight (34%) subjects were adolescents ages 13 to 17, and 301 (6%) were young children ages 0 to 5. The mean age of participants was 11.0 years with a standard deviation of 3.3. The gender composition of the sample was 75% male and 25% female. Three thousand six hundred forty-three (77%) were White, 768 (16%) were Black, six (0.1%) were American Indian/Alaskan, ten (0.2%) were Asian, 97 (2%) were Hawaiian/Pacific Islander, and 229 (5%) were Other.

Of the 2,967 subjects in the 2009 sample, 2,343 (79%) participants had a diagnosis of autistic disorder, 596 (20%) participants had a diagnosis of Asperger's disorder, and 28 (0.9%) participants had a diagnosis of an unspecified pervasive developmental disorder. With regards to comorbid diagnoses, 1,221 (41%) participants were identified as needing at least one comorbid diagnosis. The most common comorbid diagnoses were intellectual disability (19%), mood disorders (9%), attention-deficit/hyperactivity disorder (8%), communication and developmental disorders (8%), disruptive behavior disorders (4%), anxiety disorders (2%), adjustment disorders (2%), and impulse control disorders (1%). All other psychiatric comorbidities represented less than 1% of participants.

Similar to the 2001 research sample, the majority of subjects (60%) in the 2009 sample ranged from 6 to 12 years of age (N = 1,792). Five hundred ninety (20%) subjects were young

children ages 0 to 5, and 585 (20%) subjects were adolescents ages 13 to 17. The mean age of participants was 8.8 with a standard deviation of 3.8. The gender composition of the sample was 81% male and 19% female. One thousand eight hundred forty-five (62%) were White, 612 (21%) were Black, 21 (0.7%) were American Indian/Alaskan, 18 (0.6%) were Asian, 59 (2%) were Hawaiian/Pacific Islander, and 412 (14%) were Other (See Table 10. for Descriptive Statistics).

Materials

The present study utilized data retrieved from the Research Data Assistance Center (ResDAC), which provides free assistance to academic, government, and non-profit researchers interested in using Medicare or Medicaid data for their research. ResDAC is a contractor for the Center for Medicare and Medicaid Services (CMS). ResDAC employs a consortium of epidemiologists, public health specialists, health services researchers, biostatisticians, and health informatics specialists from the University of Minnesota in order to provide technical assistance to researchers interested in pursuing health service utilization data.

There are multiple strengths associated with the use of CMS administrative data for research. First, health utilization data were derived from reimbursement, or the payment of bills for health care services rendered. Information that is collected for reimbursement or the payment of bills and included within the data set was of high quality. Second, the data set includes specific information about covered services used by enrollees in the Medicaid program, including diagnoses, procedures, and sources of care. Third, extensive demographic information is provided for enrollees, such as age, date of birth, race/ethnicity, and place of residence, and all demographic information is considered largely reliable and valid. Fourth, the Medicaid data within the CMS data set represents the largest source of funding for health care services for

families with limited income in the United States. Fifty-nine percent of low-income children are insured through Medicaid or the Children's Health Insurance Program, providing health coverage to more than 43 million children. The large number of children receiving services through Medicaid allows for detailed subgroup analysis with reduced concerns about loss of statistical power. Fifth, accessing CMS data is a cost-effective way to conduct an analysis of a large segment of the population. Alternatives include requesting individual patients' medical charts, which does not allow for access to claim information across multiple providers for a given individual in a consistent reporting format, as is available within CMS records.

Despite the multiple benefits associated with the utilization of the CMS data for health care utilization research, there are limitations to utilizing insurance claims for research purposes. Different types of care may be subject to different payment rules. For example, comorbidity and severity of illness information may be inconsistently recorded if they are subject to varying payment rules. In addition, because many drugs have multiple indications, it can be difficult to interpret the reason for any given prescription. Moreover, if reimbursement rates are low, some components of treatments may not be included in billings and may not appear in claims data even if the treatment was provided. Also, if claims were not submitted for covered services, they would not be present within the data set. While these limitations were taken into consideration during the interpretation of findings from the current study, Medicaid data is frequently utilized within psychopharmacological research (Khandker & Simoni-Wastila, 1998; Mandell et al., 2002; Mandell et al., 2003; Mandell et al., 2008; Mandell et al., 2010; Ruble et al., 2008; Zito et al., 2005).

This study utilized claims records for youth with autism spectrum disorder whose health coverage was provided by Medicaid. Medicaid Analytic Extract (MAX) files provided

enrollment information and final action claims for all Medicaid beneficiaries. In order to access the database, the researcher was required to submit a formal request and data use agreement that is reviewed by ResDAC and the CMS privacy board (See Figure 3). All MAX files were requested for the purposes of this study: 1) the MAX Personal Summary File, 2) the MAX Prescription Drug File, 3) the MAX Inpatient File, 4) the MAX Long Term Care File, and 5) the MAX Other Therapy File. The objective behind collecting all MAX files was to ensure the data set would include pharmacy claims from multiple sources of care for youth diagnosed with autism spectrum disorder. Each participant was coded under a unique Beneficiary ID. Data were aggregated into a single data set for this study, with the Beneficiary IDs being used to link individual clients across data files.

The Personal Summary File contained one record for every individual enrolled in Medicaid for at least one day during the calendar year. The file primarily consisted of demographic data. The demographic data of interest in this study were date of birth, gender, race/ethnicity, and county of residence. The Personal Summary File also contained information regarding the basis of eligibility, monthly enrollment status, and a health care utilization summary. The Personal Summary File for the 2009 calendar year was composed of 7,252 beneficiary claims. A total of 12,462 insurance claims were present within the Personal Summary Files across the 2001 and 2009 calendar years (See Appendix A).

The Prescription Drug File contained final action, paid drug claims (See Appendix B). The dispensed medications were identified by a National Drug Code (NDC), which is a three-segment number that serves as a universal product identifier for drugs. The Drug Listing Act of 1972 requires registered drug establishments to provide the Food and Drug Administration (FDA) with a current list of all drugs manufactured, prepared, propagated, compounded, or

processed for commercial distribution. NDCs are available through the National Drug Code Directory (http://www.accessdata.fda.gov/scripts/cder/ndc/default.cfm). The Prescription Drug File for the 2009 calendar year was composed of 119, 991 insurance claims. A total of 150,890 insurance claims were present within the Prescription Drug Files across the 2001 and 2009 calendar years.

The Inpatient File contained records for Medicaid-enrolled youth who used inpatient hospitalization services during their eligibility period. The Inpatient File included diagnoses, procedures, discharge status, length of stay, and payment amount. The file contained up to ten diagnostic fields and seven procedure fields (See Appendix C). The Inpatient File for the 2009 calendar year was composed of 285 insurance claims. A total of 433 insurance claims were present within the Inpatient Files across the 2001 and 2009 calendar years.

The Long Term Care File contained claims for institutional long-term care services provided by nursing facilities, intermediate care facilities, and independent psychiatric facilities. The Long Term Care file included information about type, dates of services, and discharge status. In addition, the file contained up to five diagnosis codes (See Appendix D). The Long Term Care File for the 2009 calendar year was composed of 1,142 insurance claims. A total of 1,253 insurance claims were present within the Long Term Care Files across the 2001 and 2009 calendar years.

Lastly, the Other Therapy File contained records for a variety of Medicaid services, including physician services, lab/X-ray, clinic services, home health, hospice, premium payments, and outpatient hospital claims. The service utilization claims included diagnosis codes and procedure codes (See Appendix E). The Other Therapy File for the 2009 calendar year was composed of 829,250 insurance claims. A total of 1,092,515 insurance claims were present

within the Long Term Care Files across the 2001 and 2009 calendar years (See Table 11. for frequencies of claims per file type per year).

MAX files were collected for two calendar years: 2001 and 2009. Data collected from the 2009 calendar year were used to determine the prevalence of psychopharmacological treatments for youth with autism spectrum disorder, rates of polypharmacy, differential prevalence according to age group (i.e., ages 0-5, 6-11, 12-17), and differences in psychopharmacological prescribing according to autism spectrum disorder (i.e., autistic disorder, Asperger's disorder, pervasive developmental disorder not otherwise specified). Predictors of psychopharmacological utilization (i.e., age, gender, race/ethnicity, comorbid diagnoses, county demographics) were also examined using data from 2009. The year 2009 was chosen because it was the most recent calendar year available through ResDAC at the time of the study. In addition, MAX files were collected for the 2001 calendar year. The purpose of collecting an additional year of data was to describe how psychopharmacological prevalence rates have changed across time in the context of psychopharmacological research advances since the year 2000. The 2001 calendar year was chosen in order to compare current findings from the state of Michigan to a national study of psychotropic prescribing for youth with autism spectrum disorder that also utilized 2001 Medicaid data (Mandell et al., 2008).

Procedure

Data Preparation and Screening. Data preparation and screening methods followed the recommendations outlined by Raykov and Marcoulides (2008). Proofreading occurred for each variable across all subjects. Frequencies and descriptive statistics were calculated for all variables to be included in the analysis in order to locate missing data or data anomalies. If more

than five percent of the data were missing and the missing values were scattered randomly across the data set, the individual data records were deleted list-wise.

Two participants were identified with missing data for all variables of interest. Given that this data were not missing completely at random and could be attributed to two distinct participants, these participants were deleted from the analysis. In addition, 402 cases were omitted from the aggregate data set due to uncertainty regarding the participants' autism spectrum diagnosis. For example, one participant with two separate insurance claims with two different primary autism spectrum diagnoses (e.g., autistic disorder, Asperger's disorder) was identified as a case with an uncertain diagnosis. Due to diagnostic uncertainty, 191 participants were omitted from the 2001 calendar year, and 211 cases were omitted from the 2009 calendar year.

Dependent Variables. The dependent variables within the study involved pharmacy claims for psychopharmacological medications. The first dependent variable was defined as the presence or absence of a psychopharmacological pharmacy claim. It was coded as a binary variable within statistical analyses (0=Absence of psychopharmacological claim vs. 1=Presence of psychopharmacological claim). The second dependent variable was defined as the total number of psychopharmacological pharmacy claims, which was included within statistical analysis as a continuous variable.

Instances of polypharmacy were operationalized by concurrent psychotropic prescriptions that overlapped for at least 30 consecutive days. This dependent variable was coded as a binary variable (0=Absence of polypharmacy vs.1=Presence of polypharmacy) in order to identify instances of polypharmacy intervention. Other dependent variables include the presence or absence of each psychopharmacological drug class. The presence or absence of prescriptions for

each drug class was coded as separate binary variables (0=Absence of drug class vs. 1=Presence of drug class) for the purposes of statistical analysis. In addition, the total number of psychotropic agents prescribed and the total number of psychotropic medication classes prescribed were included within statistical analyses as continuous variables as additional indicators of polypharmacy intervention.

Independent Variables. The first independent variable was type of autism spectrum diagnosis. Individuals were considered to have an autism spectrum disorder diagnosis if they had at least one health care utilization claim in the year 2001 or 2009 and a listed diagnosis of autistic disorder (299.0), Asperger's disorder (299.8), or unspecified pervasive developmental disorder (299.9). Autism spectrum diagnoses were coded into separate, dichotomous variables.

The second independent variable was subject age group. Participant age was calculated using the participant's date of birth and the year associated with the dataset (i.e., 1/1/2001, 1/1/2009). Participant age was divided into three categories: 1) 0 to 5 years, 2) 6 to 12 years, and 3) 13 to17 years. For the purposes of statistical analysis, this categorical variable was recoded into separate, dichotomous variables.

The third independent variable was subject gender. Participant gender was coded as a dichotomous variable.

The fourth independent variable of interest in the study was subject race/ethnicity. Race/ethnicity was coded according to Medicaid categories, which include White, Black, American Indian/Alaskan, Asian, and Hawaiian/Pacific Islander. Race/ethnicity was coded as separate, dichotomous variables.

Many Medicaid-enrolled children with autism spectrum disorder were identified as having a comorbid diagnosis. Comorbid psychiatric disorders served as the fifth independent

variable. Other psychiatric conditions were acknowledged in the study and included within statistical analyses as separate dichotomous variables. Comorbid conditions most consistent with previous research in this area include intellectual disability, attention-deficit/hyperactivity disorders, mood disorders, and anxiety disorders according to ICD-9-CM (National Center for Health Statistics, 2002). However, all identified comorbid conditions were included within the analysis in an exploratory fashion (See Table 10. for most common comorbid diagnoses in the 2009 calendar year).

County demographic characteristics also served as independent variables within the study. County of residence was determined using the Personal Summary File. County-level demographic characteristics were determined according to the 2009 statistics publicly available through the Center for Medicare and Medicaid Services, including median household income, the percentage of White residents, the percentage of residents living in poverty, and the percentage of Medicaid-enrolled individuals ≤21 years of age. The analysis considered county education characteristics, such as total expenditures per student, the proportion of students in special education, the total number of elementary and secondary education students, and the pupil/teacher ratio. County-level educational data was located from publicly available educational data disseminated by the state of Michigan (https://www.mischooldata.org). The study also took into account county healthcare resources, including number of pediatricians and pediatric specialists, as reported by the American Academy of Pediatrics (https://www.healthchildren.org). All county demographic characteristics were divided into quartiles for ease of analysis, which is consistent with previous research regarding the effect of demographic variables on the treatment of mental health disorders.

*Research Question 1***.** The prevalence of psychopharmacological treatments for Medicaid-enrolled youth with autism spectrum disorder was determined by analyzing the frequency of and percentage of youth being prescribed psychopharmacological medications during the 2009 calendar year. The general prevalence (i.e., the presence or absence) of a psychopharmacological prescription was reported using descriptive statistics. Prevalence rates were also calculated to represent the percentage of the sample receiving psychopharmacological intervention within each psychotropic medication class (i.e., atypical antipsychotics, stimulants, antidepressants, alpha-2 agonists, anticonvulsants, traditional antipsychotics, and miscellaneous anxiolytics/sedatives/hypnotics). Prevalence of psychopharmacological intervention was further analyzed according to autism spectrum disorder diagnosis (i.e., autistic disorder, Asperger's disorder, pervasive developmental disorder not otherwise specified) and age group (i.e., ages 0-5, 6-12, 13-17) using descriptive statistics.

Research Question 2. The prevalence of polypharmacy among Medicaid-enrolled youth with autism spectrum disorder was determined using descriptive statistics. Prevalence rates were calculated across all participants based on the presence or absence of polypharmacy, which was operationally defined as two or more concurrent psychotropic prescriptions that overlap for a minimum of 30 days. The frequency and percentage of participants receiving polypharmacy intervention during the 2009 calendar year was calculated. The prevalence of polypharmacy was further analyzed according to autism spectrum disorder diagnosis (i.e., autistic disorder, Asperger's disorder, pervasive developmental disorder not otherwise specified) and age group (i.e., ages 0-5, 6-12, 13-17) using descriptive statistics.

Research Question 3. The predictive value of subject age (Age Group 1: 0-5, Age Group 2: 6-12, Age Group 3: 13-17) on psychopharmacological prescribing practices for Medicaid-

enrolled youth with autism spectrum disorder was analyzed using generalized linear modeling (negative binomial regression) and logistic regression techniques. Dependent variables included the presence or absence of a psychopharmacological prescription, the presence of absence of polypharmacy intervention, the presence or absence of each medication class, the total number of psychopharmacological prescriptions prescribed, the total number of psychotropic agents prescribed, and the total number medication classes prescribed. Age group served as the independent variable of interest. Other independent variables (i.e., gender, race/ethnicity, autism spectrum disorder diagnosis, presence of comorbid diagnoses, and county demographics) were entered into the generalized linear model as covariates to increase statistical control. To account for the number of dependent variables being regressed against each participant, a Bonferroni adjustment was conducted to ensure a conservative interpretation of statistical outcomes and reduce Type-1 error. As a result, statistical significance was evaluated at a $p \leq 0.004$.

The effect of age on psychopharmacological prescribing practices was further analyzed using logistic regression techniques. According to Hosmer and Lemeshow (2000), logistic regression is used to analyze relationships between a dichotomous dependent variable and other independent variables. This method computes the probability that a case with a particular set of values for an independent variable is a member of the modeled category. In this study, the predictive value of the independent variables (i.e., age, gender, race/ethnicity, autism spectrum diagnosis, comorbid diagnoses, county demographics) on psychotropic drug use was investigated. During statistical analyses, the presence or absence of any psychopharmacological prescription, the presence or absence of polypharmacy, and the presence or absence of each psychotropic drug class served as dichotomous dependent variables.

The value produced by logistic regression is a probability value between 0.0 and 1.0. If the probability for group membership in the modeled category (e.g., female) is above a pre-specified cut point, the subject is predicted to be a member of the modeled group (e.g., presence of psychotropic medication). If the probability for group membership in the modeled category is below a pre-specified cut point, the subject is predicted to be a member of the other group (e.g., absence of psychotropic medication) (Raykov & Marcoulides, 2008).

Research Question 4. In order to analyze whether autism spectrum disorder diagnosis (i.e., autistic disorder, Asperger's disorder, unspecified pervasive developmental disorder) was a significant predictor of psychopharmacological prescribing practices for Medicaid-enrolled youth in the 2009 calendar year, generalized linear modeling (negative binomial regression) and logistic regression techniques were conducted. Autism spectrum diagnosis served as the independent variable of interest with regards to its effect on the dependent variables (i.e., presence or absence of a psychopharmacological prescription, presence of absence of polypharmacy intervention, presence or absence of each medication class, total number of psychopharmacological prescriptions prescribed, total number of psychotropic agents prescribed, total number medication classes prescribed). All other independent variables (i.e., age, gender, race/ethnicity, comorbid diagnoses, county demographics) were included within the model to increase statistical control within the model.

Research Question 5. The predictive value of comorbid diagnoses (e.g., intellectual disability, attention-deficit/hyperactivity disorder, mood disorders, anxiety disorders) on the presence or absence of a psychopharmacological prescription, the presence or absence of polypharmacy intervention, the total number of psychopharmacological prescriptions prescribed, the total number of psychotropic agents prescribed, and the total number of medication classes

prescribed was analyzed using generalized linear modeling (negative binomial regression) and logistic regression techniques. The remaining independent variables, including age, gender, race/ethnicity, county demographics, were controlled for within the generalized linear model.

Research Question 6. In order to determine if demographic characteristics, including gender, race/ethnicity, and county demographics, served as significant predictors of psychopharmacological prevalence among Medicaid-enrolled youth with autism spectrum disorder in the state of Michigan in the 2009 calendar year, generalized linear modeling (negative binomial regression) and logistic regression techniques were utilized. All independent variables were controlled for within the generalized linear model.

Research Question 7. In order to examine if psychotropic medication rates increased among Medicaid-enrolled children with autism spectrum disorder between years 2001 and 2009, psychotropic prevalence rates were calculated for 2001 and 2009. Prevalence calculations included the presence or absence of any psychopharmacological prescription, the presence or absence of polypharmacy, and the presence or absence of each medication class. Fold increases were calculated from 2001 to 2009 in order to make inferences regarding change over time in psychopharmacological prescribing for Medicaid-enrolled youth with autism spectrum disorder.

Chapter 4:

Results

*Research Question 1***.** The first research question examined the prevalence of psychopharmacological treatments for Medicaid-enrolled youth with autism spectrum disorder for the 2009 calendar. The total sample consisted of 2,967 participants. Approximately 60% (*N*=1782) of participants were prescribed a psychopharmacologic medication in 2009. Further analysis according to medication class indicated that atypical antipsychotics, stimulants, and alpha-2 agonist medications were the most frequently prescribed medication classes. More specifically, approximately 34% were prescribed atypical antipsychotics, 33% were prescribed stimulants, and 20% were prescribed alpha-2 agonists (See Figure 4 for prevalence rates of all psychotropic agents).

Psychotropic prevalence rates were further analyzed according to autism spectrum disorder diagnosis. Medicaid-enrolled youth with Asperger's disorder (66%) had a higher prevalence rate of being prescribed a psychotropic medication than Medicaid-enrolled youth with autistic disorder (59%) and pervasive developmental disorder (50%). The most commonly prescribed medication classes for youth with autistic disorder were atypical antipsychotics (33%), stimulants (32%), and alpha-2 agonists (20%), while the most commonly prescribed medication classes for youth with Asperger's disorder were atypical antipsychotics (38%), stimulants (38%), and antidepressants (23%).

Further analysis of psychotropic prevalence rates according to age group indicated that teenagers ages 13 to 17 had the highest rates of psychopharmacologic prescribing with a prevalence rate of 73%, followed by children ages 6 to 12 with a prevalence rate of 63% and young children ages 0 to 5 with a prevalence rate of 38%. For young children ages 0 to 5, atypical antipsychotics (16%), alpha-2 agonists (15%), and miscellaneous anxiolytics, sedatives,

and hypnotics (11%) were the most commonly prescribed medication classes. For children ages 6 to 12, stimulants (39%), atypical antipsychotics (37%), and alpha-2 agonists (23%) were the most commonly prescribed medication classes. Lastly, atypical antipsychotics (44%), stimulants (37%), and antidepressants (36%) were the most commonly prescribed medication classes for children ages 13 to 17 (See Table 12.).

Research Question 2. The second research question examined the prevalence of polypharmacy for Medicaid-enrolled youth during the 2009 calendar year. Descriptive statistics indicated that approximately 36% of participants were prescribed two or more concurrent psychotropic medications. Polypharmacy intervention was found to be more prevalent in youth with a diagnosis of Asperger's disorder than in youth with a diagnosis of autistic disorder (40% vs. 35%, respectively). With regards to age group, polypharmacy intervention was most prevalent in adolescents ages 13 to 17 (52%) compared to youth ages 6 to 12 (39%) and 0 to 5 (12%) (See Table 2.)

Research Question 3. The third research question investigated the predictive value of age group on psychopharmacological prescribing practices for Medicaid-enrolled youth with autism spectrum disorder. Resulting odds ratios within logistic regression analyses indicated that children in older age groups (i.e., ages 6-12, ages 13-17) were significantly more likely to be prescribed a psychotropic medication than young children (i.e., ages 0-5). More specifically, children ages 6 to 12 were approximately 3 times more likely and youth ages 13 to 17 were approximately 4 times more likely to be prescribed a psychopharmacologic script than young children ages 0 to 5 (See Table 13.).

Similarly, older children were significantly more likely than younger children to be prescribed polypharmacy intervention. Children ages 6 to 12 were approximately 5 times more

likely and children ages 13-17 were approximately 8 times more likely than young children ages 0-5 to be prescribed polypharmacy intervention (See Table 14.). When all other predictor variables were held constant using negative binomial regression techniques, statistically significant differences were found between young children ages 0 to 5 and children in older age groups for total number of psychopharmacologic scripts (See Table 15.), total number of psychopharmacologic agents (See Table 16.), and total number of psychopharmacologic classes prescribed (See Table 17.).

Furthermore, odds ratios according to medication class identified a similar trend across age groups, with older children (i.e., ages 6-12, ages 13-17) being significantly more likely to be prescribed agents in the stimulant [Ages 6-12: $OR = 6.571$] [Ages 13-17: $OR = 5.931$], atypical antipsychotic [Ages 6-12: $OR = 2.972$] [Ages 13-17: $OR = 4.032$], antidepressant [Ages 6-12: $OR = 6.577$] [Ages 13-17: $OR = 15.514$], anticonvulsant [Ages 6-12: $OR = 2.520$] [Ages 13-17: $OR = 5.140$], and antipsychotic [Ages 6-12: $OR = 13.738$] [Ages 13-17: $OR = 47.250$] medication classes at the $p < 0.001$ significance level. With regards to being prescribed the alpha-2 agonist class, children in the 6 to 12 age group were significantly more likely to be prescribed an alpha-2 agonist agent ($OR = 1.694$, $p < .001$) than young children ages 0 to 5. While teenagers were found to be more likely to receive an alpha-2 agonist agent descriptively, differences in alpha-2 agonist prescribing were not statistically significant [$OR = 1.324$, $p = 0.075$]. In contrast, young children ages 0 to 5 were more likely to be prescribed agents in the miscellaneous anxiolytic, sedative, and hypnotic class than youth in older age groups; however, the likelihood of being prescribed this medication class was only statistically significant between children in the 0-5 and 6-12 age group ($OR = 0.676$, $p = 0.015$].

Research Question 4. The fourth research question analyzed the predictive value of autism spectrum diagnosis (i.e., autistic disorder, Asperger's disorder) on psychopharmacological prescribing practices. Participants with a diagnosis of pervasive developmental disorder were omitted from the analyses due to low sample size ($N = 28$). Youth with diagnoses of Asperger's disorder were significantly more likely to be prescribed a psychotropic medication (See Table 13.) compared to youth with diagnoses of autistic disorder. With regards to prescribing practices by medication class, youth with diagnoses of autistic disorder were significantly less likely to be prescribed antipsychotics [$OR = 0.547$, $p = 0.001$] than youth with diagnoses of Asperger's disorder.

Research Question 5. The predictive value of comorbid diagnoses on psychopharmacological prescribing practices was also assessed within the study. Youth with autism spectrum diagnoses and comorbid diagnoses were found to be prescribed more total psychopharmacologic prescriptions (See Table 15.) and more total psychotropic agents (See Table 16.) compared to youth with autism spectrum disorder without comorbid diagnoses when all other independent predictors were held constant. Logistic regression analyses indicated that participants with comorbid diagnoses were significantly more likely to be prescribed polypharmacy intervention (See Table 14.) than participants without comorbid diagnoses.

Additionally, logistic regression analytic techniques also provided information regarding the effect of comorbid diagnoses on the likelihood of being prescribed agents various medication classes. Participants with comorbid diagnoses were found to be significantly more likely to be prescribed atypical antipsychotic [$OR = 1.326$, $p < .001$], antidepressant [$OR = 1.474$, $p < .001$], anticonvulsant [$OR = 1.585$, $p < .001$], alpha-2 agonist [$OR = 1.305$, $p = 0.004$], and antipsychotic [$OR = 1.824$, $p < .001$] agents.

The predictive value of specific comorbid disorders on psychopharmacologic prescribing practices was also examined in an exploratory fashion using logistic regression. Participants with a comorbid diagnosis of a mood disorder [*OR* = 1.926, $p < .001$] were approximately twice as likely to be prescribed a psychopharmacologic prescription compared to participants without this comorbid diagnosis. Participants with a comorbid diagnosis of a mood disorder were approximately three times as likely [*OR* = 2.856] than those without this comorbid diagnosis to receive polypharmacy intervention, and participants with a comorbid diagnosis of a disruptive behavior disorder were approximately twice as likely [*OR* = 2.044, $p < .001$] to receive polypharmacy intervention.

The predictive value of comorbid diagnoses was also assessed according to medication class. Within logistic regression analyses, a participant was significantly more likely to be prescribed atypical antipsychotics if the participant had a comorbid diagnosis of a mood disorder [*OR* = 2.325, $p < .001$] or a disruptive behavior disorder [*OR* = 1.824] compared to those without these disorders. Participants were significantly more likely to be prescribed antidepressants if the participant had a comorbid diagnosis of a mood disorder [OR = 2.859, $p < .001$] or a disruptive behavior disorder [*OR* = 1.999, $p < .001$]. Participants were more likely to be prescribed anticonvulsants if the participant had a comorbid diagnosis of intellectual disability [*OR* = 1.514, $p < .001$], a communication/developmental disorder [*OR* = 1.721, $p < .001$], a mood disorder [*OR* = 2.514, $p < .001$], or a disruptive behavior disorder [*OR* = 2.403, $p < .001$] than participants without these disorders. Participants were more likely to be prescribed an alpha-2 agonist agent if the participant had a comorbid diagnosis of a mood disorder [*OR* = 1.728, $p < .001$] or attention/deficit/hyperactivity disorder [*OR* = 1.690, $p < .001$] than those without these disorders. Lastly, participants were more likely to be prescribed antipsychotic agents if the participant had a

comorbid diagnosis of a mood disorder [$OR = 4.067$, $p < .001$], a disruptive behavior disorder [$OR = 3.722$, $p < .001$], or an impulse control disorder [$OR = 3.656$, $p = 0.002$].

Research Question 6. The effects of individual and county-level demographic characteristics on psychopharmacologic prescribing practices were analyzed using logistic and negative binomial regression. Logistic regression analysis indicated that gender did not significantly predict the likelihood of being prescribed a psychopharmacologic prescription (See Table 13.) or polypharmacy intervention (See Table 15.). However, females were found to be significantly less likely to be prescribed stimulant medications [$OR = 0.636$, $p < .001$] than males. Descriptive statistics indicated that approximately 35% of males were prescribed stimulants versus approximately 25% of females. No significant differences were found between males and females for total number of psychopharmacologic scripts, total number of psychotropic agents, or total number of medication classes prescribed during the 2009 calendar year when controlling for covariates using negative binomial regression (See Tables 15., 16., 17.).

Logistic regression also identified Black children as being significantly less likely to be prescribed a psychopharmacologic prescription (See Table 13.), polypharmacy intervention (See Table 14.), stimulants [$OR = 0.577$, $p < .001$], atypical antipsychotics [$OR = 0.741$, $p = 0.003$], antidepressants [$OR = 0.391$, $p < .001$], anticonvulsants [$OR = 0.646$, $p = 0.001$], and alpha-2 agonists [$OR = 0.684$, $p = 0.002$] (See Table 12.) when compared to White children. When controlling for all other independent variables using negative binomial regression, White children were found to be prescribed significantly more psychopharmacologic scripts (See Table 15.), psychopharmacologic agents (See Table 16.), and medication classes (See Table 17.) compared to Black children. Significant differences were also found between children who

identified as White and Hawaiian/Pacific Islander for total number of scripts prescribed (See Table 15.), which White children being prescribed significantly more prescriptions than children identified as Hawaiian/Pacific Islander. However, these results should be interpreted with caution due to significant differences in sample size between these two racial groups.

Analyses of county education characteristics identified that the total number of students and student/teacher ratio had a significant effect on psychopharmacologic prescribing practices for Medicaid-enrolled youth in the state of Michigan. Participants within the second quartile with regards to total number of students were found to be significantly more likely to receive a psychopharmacologic claim than participants in the quartile that represented the fewest number of students (See Table 13.). Descriptively, approximately 64% of participants in the second quartile were prescribed a psychopharmacologic agent compared to approximately 58% of participants in the lowest quartile.

Total number of students was also found to significantly influence prescribing practices for atypical antipsychotics. Students in the second quartile [$OR = 1.342$, $p = 0.001$] were found to be significantly more likely to receive an atypical antipsychotic than participants in the lowest quartile. Approximately 38% of participants in the second quartile were prescribed atypical antipsychotics compared to approximately 31% of participants in the lowest quartile.

Results of negative binomial regression analyses indicated that student/teacher ratio had a significant effect on prescribing practices for Medicaid-enrolled youth. Participants in the fourth quartile, which represented low student/teacher ratio, received significantly fewer total psychopharmacologic scripts than participants in the first quartile, which represented high student/teacher ratio. Participants in the quartile with the lowest student/teacher ratio were also

found to be significantly less likely to receive an anticonvulsant prescription [Q4: $OR = 0.343$, $p = 0.004$) compared to participants in the quartile with the highest student/teacher ratio.

While certain county education characteristics were found to significantly predict psychopharmacologic prescribing practices within the sample, not all education characteristics were found to be significantly associated with psychopharmacological prescribing practices. Results of statistical analyses suggested that neither total student expenditures nor proportion of students in special education were significantly associated with prescribing practices. Logistic regression analyses indicated that no significant differences were found for upper quartiles when compared to the lowest quartile for the presence of a psychopharmacologic claim, presence of polypharmacy intervention, or the presence of any medication class for these variables. Furthermore, results of negative binomial regression suggested that the predictive value of the level of total student expenditures and the proportion of students in special education were insignificant.

Within the investigation of the effect of county healthcare characteristics on prescribing practices, the predictive value of number of pediatricians or pediatric specialists on dependent variables was analyzed. This county healthcare characteristic was not found to have a significant effect on prescribing practices for Medicaid-enrolled children in Michigan in the 2009 calendar year.

Lastly, the effect of county demographic characteristics on psychopharmacologic prescribing was analyzed, including median household income, percentage of White residents, percentage of the population living in poverty, and percentage of Medicaid-enrolled youth. Results of logistic regression analyses did not identify any significant differences in any quartile when compared to the lowest quartile for any of the aforementioned demographic characteristics

on the presence of a psychopharmacologic prescription, presence of polypharmacy intervention, or presence of any psychotropic medication class.

Research Question 7. Analyses examining the differences in psychopharmacologic prescribing over time for Medicaid-enrolled youth with autism spectrum disorder found that overall prevalence rates approximately doubled between the years 2001 (32% prevalence) and 2009 (60% prevalence). A substantial increase in the prevalence rate of polypharmacy intervention was also observed. Prevalence rates of polypharmacy intervention increased from approximately 14% in 2001 to approximately 36% in 2009.

Moreover, analyses investigating differences in prescribing practices per medication class identified two-fold increases in prevalence rates for stimulant, antidepressant, and anticonvulsant agents between 2001 and 2009. Three-fold increases were observed in prevalence rates for atypical antipsychotics and miscellaneous anxiolytics, sedatives, and hypnotics. Lastly, a dramatic six-fold increase was observed for the prevalence of alpha-2 agonist agents during the targeted decade (See Figure 5).

Chapter 5:

Discussion

The prevalence rate of psychopharmacological prescribing that was identified in the current study for youth with autism spectrum disorder was dramatic. The overall prevalence rate of 60% receiving medication management of behaviors associated with autism spectrum disorder far exceeded prevalence rates reported by prior studies of psychopharmacological prescribing, which yielded psychotropic prevalence rates between 39% (Aman et al., 1995) and 46% (Aman et al., 2003; Langworthy-Lam et al., 2002). However, given the state-level focus and breadth of socioeconomic levels present within previous studies, caution should be taken when making direct comparisons between the present study and prior research. However, the 60% prevalence rate in the current study exceeded the prevalence rate of 56% that was found in an earlier national study of Medicaid-enrolled youth with autism spectrum disorder (Mandell et al., 2008), which was the most generalizable research study to the sample within the present study. Observed increases in psychotropic prescribing are consistent with increases in psychotropic medication use that has been observed in other clinical populations of youth (Zito et al., 2000).

The observed increase in psychopharmacological prescribing may be explained by the substantial amount of research literature that was published regarding the safety, efficacy, and tolerability of psychotropic medication use for children and adolescents with autism spectrum disorder that has been completed since the year 2000. The research evidence for atypical antipsychotics, particularly risperidone (Aman et al., 2005; McCracken et al., 2002; Shea et al., 2004; Troost et al., 2005) and aripiprazole (Aman et al., 2010; Marcus et al., 2009; Owen et al., 2009), became of sufficient quality and quantity to lead to the FDA approval of risperidone in 2006 and aripiprazole 2009 for the treatment of irritability associated with this disorder. The

findings within the current study mirrored these research advances, with the most commonly prescribed medication class being atypical antipsychotics, which were being prescribed to approximately 34% of youth with autism spectrum disorder.

Despite research indicating that atypical antipsychotics are safe and efficacious treatments for the irritability associated with autism spectrum disorder, gaps in the research literature persist. With regards to both risperidone and aripiprazole, the research literature has primarily investigated the short-term and intermediate-term effects of these agents for the treatment of irritability within this population. As a result, the long-term effects of utilization of these agents in developing children are unknown. Further, more research is needed to determine the minimally tolerated and maximally tolerated doses for each of these agents in order to inform clinical practice and minimize potential side effects. Despite FDA approval and in the context of the aforementioned limitations, caution is warranted surrounding use of atypical antipsychotics within this clinical population.

Although atypical antipsychotics were found to be the most prevalent psychotropic medication class in 2009 within the current study, stimulant medication (33%) reached a similar prevalence rate. While prior research indicated modest improvements in hyperactivity (Handen et al., 2000; Quintana et al., 1994; RUPP, 2005) and stereotypies (Handen et al., 2000) for the population of youth taking methylphenidate medication, significant side effects were observed (Handen et al., 2000; RUPP, 2005). As a result, a conservative approach is advised when prescribing this medication to youth with autism spectrum disorder. However, given that side effects occur quickly after stimulant medication is initiated, clinicians are able to immediately assess the tolerability of the medication for these children.

Also with regards to stimulant medication, it is also important to note that according to the RUPP (2005) study of the efficacy and safety of stimulant medication for youth with autism spectrum disorder, the percentage of positive responders to methylphenidate was less for children with autism spectrum disorder (49% positive response) than for youth with attention-deficit/hyperactivity disorder (70-80% positive response) (Greenhill et al., 2001). While stimulant medication has some research support for the treatment for hyperactivity associated with attention-deficit/hyperactivity disorder, it appears that children on the autism spectrum have a relatively less favorable response to this medication.

Alpha-2 agonist agents were the most prevalent medication class following atypical antipsychotics and stimulants within the current study. While controlled research has suggested that clonidine has beneficial effects on overall behavior, social relationships (Fankhauser et al., 1992), and hyperactivity (Jaselskis et al., 1992) associated with autism spectrum disorder, research is significantly limited by small sample sizes and inconsistent findings. Despite the limited research base, antiadrenegic agents were prescribed to 20% of the research sample within this population, which represents an 8-fold increase from the prevalence rate reported in a Medicaid-enrolled sample of youth with autism spectrum disorder in 2001 (3%) (Mandell et al., 2008). Awareness of this substantial increase in the setting of the research evidence is important for clinician when considering prescribing this medication class to youth with autism spectrum disorder.

A striking finding within the current research study was the prevalence rate found for polypharmacy (36%), which far exceeded the 20% prevalence rates reported within previous studies of children with autism spectrum disorder (Aman et al., 2003; Mandell et al., 2008).While research has blossomed since the year 2000 with regards to the safety and efficacy

of specific psychotropic agents on symptoms associated with autism spectrum disorder, the current state of the literature is devoid of research regarding usage of multiple, concurrent psychotropic medication within developing children with autism spectrum disorder. However, polypharmacy intervention continues to be a common practice within the state of Michigan for Medicaid-enrolled youth with these disorders.

With regards to subsets of the population on the autism spectrum, the current study suggests that prevalence rates within all age groups exceeded prevalence rates identified within previous research of youth with autism spectrum disorder (Aman et al., 1995; Aman et al., 2003; Langworthy-Lam et al., 2002; Mandell et al., 2008). Arguably, the most notable finding within the study includes the high prevalence rate found within youth in early childhood, which reached approximately 38%. Factors that may be influencing this increase in prevalence includes greater awareness of autism spectrum disorder, focus on early identification of the disorder, and an increase in prevalence rates of psychotropic prescribing for young children within clinical populations outside of the realm of autism spectrum disorder (Zito et al., 2000). However, the increasing prevalence rate of psychotropic prescribing for this population of young children must be framed in the context of the paucity of research regarding the safety and efficacy of psychotropic medication use among early childhood populations. No randomized controlled trials have been conducted to validate use of psychotropic medications for this age group; therefore, this treatment practice has not been established as safe or efficacious for this developmental period.

It was hypothesized within the current study that older age would predict greater use of psychotropic medication for the treatment of autism spectrum disorder. Support for this hypothesis was found within the current study. Adolescents were found to have the highest rates

of psychopharmacological prescribing. Approximately three quarters of Medicaid-enrolled adolescents with autism spectrum disorder received medication management of symptoms in the state of Michigan in 2009, which exceeded the 67% prevalence rate previously reported in 2001 (Mandell et al., 2008).

Several factors may play a role in these age-related trends, with psychotropic prescribing peaking in adolescence. First, some comorbid psychiatric conditions tend to occur later in development, such as anxiety and depression. Mood disorders particularly occur in individuals on the autism spectrum at an age at which they are able to recognize their level of impairment. Second, there may be a greater need for psychotropic medications as children on the autism spectrum age and experience increases in height and weight. As children become physically larger, the behaviors associated with autism spectrum disorder, such as irritability, aggression, hyperactivity, and self-injurious behavior, may pose a greater risk to these individuals and to those around them. As a result, there may be an increase in the perceived need for psychotropic medications to treat the associated behaviors due to safety concerns.

Further examination of the effect of age on prescribing practices indicated that the most commonly prescribed medication classes varied according to age group. The most commonly prescribed medication classes for youth ages 0 to 5 were atypical antipsychotics, alpha-2 agonists, and miscellaneous anxiolytics, sedatives, and hypnotics, respectively. It is important to recognize that the foundation for the FDA approval of atypical antipsychotic medication included randomized controlled trials that did not include young children ages 0 to 5. As a result, risperidone is FDA-approved for children ages 5 and older, and aripiprazole is FDA-approved for children ages 6 and older. Despite these age designations, atypical antipsychotics were among the most frequently prescribed psychotropic agents during the early childhood period.

The most commonly prescribed medication classes prescribed for youth ages 6 to 12 were stimulants, atypical antipsychotics, and alpha-2 agonists, respectively. Finally, the most commonly prescribed medication classes for youth ages 13 to 17 were atypical antipsychotics, stimulants, and antidepressants, respectively. This finding is valuable because it may help to describe the unique mental and behavioral health needs for each age group. For example, stimulants appear to be the most commonly prescribed agent within the developmental period during which children typically begin attending formal elementary schooling, when new environmental demands are placed on youth (e.g., sitting still, remaining quiet, attending to instruction). Similarly, antidepressants are only among the most commonly prescribed agents for adolescents, which may be attributable to mood and anxiety concerns that can arise during the teenage years for this population.

While previous research regarding the effect of gender on psychopharmacological prescribing practices is largely inconclusive for youth with autism spectrum disorder, a previous study of general psychopharmacology among youth found that males were more likely to be prescribed psychotropic medications (Martin et al., 2003). While the present study did not identify significant differences between males and females with regards to the presence of psychopharmacological intervention or the presence of polypharmacy, males were found to be more likely to receive a stimulant medication than females. This association is consistent within findings from the national study of Medicaid-enrolled youth with autism spectrum disorder (Mandell et al., 2008). The study reported that while the percentages of youth being prescribed psychotropic medication were similar across genders (55% of females vs. 56% of males), males were more likely to be prescribed stimulant medication than females (24% of males vs. 17% of females).

This finding could be attributable to the epidemiological characteristics of attention-deficit/hyperactivity, a common psychiatric comorbidity that occurs alongside autism spectrum disorder. Attention-deficit/hyperactivity disorder is more prevalent in males than in females, and a commonly used intervention for attention-deficit/hyperactivity disorder is stimulant medication. Therefore, the association found within the current study between males with autism spectrum disorder and stimulant medications may be influenced by the treatment of this comorbidity.

However, these gender-related effects should be interpreted with caution due to the small percentages of females within this study and previous studies in comparison to males, which represents the gender distribution of the disorder itself. It has been reported that the rate of autism is four to five times higher in males than in females (American Psychiatric Association, 2000). This gender-related statistic is commensurate with the gender distribution within the current study, with approximately four times as many males (81%) than females (19%) within the research sample.

Significant racial disparities were also observed with regards to psychopharmacological prescribing practices in the state of Michigan in 2009. Black children were found to be significantly less likely to receive a psychotropic prescription, polypharmacy intervention, and most medication classes when compared to their White counterparts. Black children were also found to receive significantly fewer total prescriptions, total agents, and total medication classes than White children. Although autism spectrum disorder occurs equitably across demographic groups (Dyches et al., 2004), the findings within the current study support prior research suggesting that racial and ethnic disparities lead to differences in the medical management of symptoms within the population of youth with autism spectrum disorder (Mandell et al., 2008),

as well as within the general population of youth requiring medication for the purposes of mental health (Zito et al., 2008).

While racial and ethnic disparities in diagnosis and access to care may have influenced the identified association between race/ethnicity and psychopharmacological treatment, racial and ethnic differences in the pursuit of and trust in the mental health care system may have influenced the current findings (Matthews & Hughes, 2001). Moreover, skepticism within African American culture surrounding the safety, efficacy, and acceptance of psychotropic medications may have contributed to the current findings (Schnittker, 2003). However, due to small sample sizes within the remaining racial groups, further research is needed in order to more fully inform how race/ethnicity plays a role in psychotropic prescribing for youth on the autism spectrum.

A consistency found between the current study and previous research includes the influence of individual characteristics on prescribing practices, such as type of autism spectrum disorder and the presence of comorbidities. Youth in this study with a diagnosis of Asperger's disorder were found to be more likely to be prescribed a psychopharmacological script than children with a diagnosis of Autistic disorder. In the study by Martin and colleagues (1999) that investigated the psychotropic prevalence rates among higher-functioning individuals with autism, similar findings were identified. One explanation proposed for this finding includes that higher-functioning individuals may be more aware of their social-emotional differences compared to their typically-developing peers. As a result, higher functioning individuals on the autism spectrum, such as those given the historical diagnosis of Asperger's disorder, may be more likely to express mood and adjustment difficulties that lead medical professionals to prescribe medication management of mood and anxiety symptoms.

Despite the finding that youth with Asperger's disorder were more likely to receive a psychopharmacologic script than youth with Autistic disorder, it is important to highlight that the type of autism spectrum disorder diagnosis did not have a significant effect on the total number of scripts prescribed, the total number of agents prescribed, the presence of polypharmacy, the total number of classes prescribed, or the majority of medication classes prescribed. One factor that may have influenced these insignificant findings includes the lack of diagnostic clarity that can occur between these historical diagnoses given the high complexity and variability in the behavioral presentation of youth on the autism spectrum.

The present study also identified that youth with psychiatric comorbidities were significantly more likely to receive polypharmacy intervention, as well as more likely to receive several medication classes (i.e., atypical antipsychotics, antidepressants, anticonvulsants, alpha-2 agonists, antipsychotics). With regards to specific comorbid diagnoses, this research study and previous research studies identified that this diagnostic feature significantly influences psychopharmacologic prescribing practices, with intellectual disability, attention-deficit/hyperactivity disorder, depression, and anxiety being commonly associated with autism spectrum disorder. The common occurrence of psychiatric comorbidities highlights the complexity of clinic characteristics carried by this population. Despite the high prevalence of medication utilization for youth with psychiatric comorbidities, the research suggests that 30% of parents feel as though their child's developmental needs are still not being met (Zablotsky et al., 2015).

Interestingly, the current study suggests that youth with a comorbid diagnosis of intellectual disability are not more likely to be prescribed a psychopharmacological agent as suggested in the literature (Aman et al., 1995; Aman et al., 2003; Langworthy et al., 2002).

Limitations to the findings regarding the relationship between intellectual disability and psychotropic prescribing are two-fold. First, there is the potential for inconsistent reporting of intellectual disability as a comorbid diagnosis. For example, insurance-related billing primarily involves diagnostic coding according to primary diagnosis. As such, clinicians who are billing to insurance may not include supplementary diagnoses for individuals with an established primary diagnosis (e.g., autism spectrum disorder) because it is not required. As a result, secondary diagnoses, such as intellectual disability, may be inconsistently reported within the insurance claim data used in the current study. Secondly, due to cognitive deficits that can be inherent within an autism spectrum disorder diagnosis, intellectual disability may not have been further identified by a subsequent intellectual disability diagnosis.

Yet, participants with a comorbid diagnosis of an intellectual disability were found to be significantly more likely to receive an anticonvulsant medication than those without this diagnosis. Due to the fact that intellectual disability can be an associated feature of autism spectrum disorder, it may not always be listed as a secondary diagnosis within insurance-related billings. It is possible that clinicians take additional care to list a secondary diagnosis of intellectual disability if it is moderate to severe. If this assumption is true, the identified association between intellectual disability and anticonvulsant medications may support prior research findings that individuals with moderate to profound intellectual disability were significantly more likely to receive anticonvulsant medication than those with less severe intellectual disability (Aman et al., 1995).

The significant effects of county educational characteristics, particularly the total number of students and student/teacher ratio, on psychopharmacologic prescribing practices are noteworthy findings within the current study. Through descriptive statistics, further examination

of the effect of total student count on the likelihood of being prescribed a psychotropic medication indicated that children in the second and third quartile had a higher percentage of participants being prescribed a psychotropic prescription than participants in the lowest quartile or the highest quartile. In other words, counties with low student counts and counties with high student counts were less likely to receive a psychotropic medication.

Several explanations are proposed behind the relationship between student population and psychopharmacological prescribing practices. First, counties with lower student counts may allow for more individualized behavioral interventions for children, which may lessen the perceived need for medication management of behavioral symptoms. Second, counties with lower student counts may also represent rural areas or areas with low population density, which may lessen availability of healthcare.

On the other hand, counties with high student counts may limit the ability of school personnel to meet the high needs of children within this population. As a result, school personnel might be less likely to refer families of these youth to pediatricians and pediatric specialists for the consideration of a comprehensive treatment plan involving behavioral and medical components. In contrast, it is also possible that counties with high student counts have greater financial means and more resources to develop and implement behavioral intervention strategies in the school setting; therefore, there may be a less of a perceived need to refer families for medical management of the behaviors associated with autism spectrum disorder. These potential explanations are hypotheses that cannot be substantiated because they are outside of the scope of the current study.

Furthermore, student/teacher ratio was found to be significantly associated with the total number of prescriptions for participants within the study. Participants in a county with the lowest

student/teacher ratio received significantly fewer total psychopharmacological scripts than participants in counties with the highest student/teacher ratio. Low student/teacher ratio may allow schools to provide more individualized attention to the specific needs of youth with autism spectrum disorder and implement more tailored interventions to meet the specific behavioral needs of these children. In contrast, given the large number of students that require attention from teachers within counties with a high student/teacher ratio, teachers may be less likely to satisfy the high level of behavioral needs that can present for young children with autism spectrum disorder, thus making the perceived need for psychopharmacological intervention more likely.

Student/teacher ratio may also be influenced by population density within specific counties. Less densely populated areas may lead to lower student/teacher ratios, as well as more limited access to healthcare services. Therefore, population density may contribute to families within low-density areas receiving fewer psychopharmacological scripts when compared to more densely populated areas with greater access to healthcare resources.

An unanticipated finding within the current study includes the insignificant effects of county-level demographic characteristics and county healthcare characteristics on psychopharmacological prescribing practices. Although previous research has suggested that economically disadvantaged communities were associated with lower rates of autism identification and decreased access to healthcare services (Liptak et al., 2008), county demographic variables and county healthcare resources were not found to have a significant effect on psychopharmacological prescribing practices for Medicaid-enrolled youth with autism spectrum disorder. However, methodological limitations may play a role in this negative finding (See Limitations).

Lastly, the results of this study indicated a dramatic increase in prevalence of psychopharmacologic intervention to treat the symptoms of autism spectrum disorder in the state of Michigan between 2001 and 2009. Based on comparisons made between the current study and the most generalizable study in the research literature surrounding Medicaid-enrolled youth with autism spectrum disorder (Mandell et al., 2008), prescribing practices appear to have significantly increased in the setting of the research advances since the year 2000 with regards to the safety and efficacy of psychotropic agents for the treatment of behaviors associated with the disorder. Fold-increase estimates further suggest that each medication class at least doubled between 2001 and 2009 with the exception of traditional antipsychotics, which have been found to be associated with significant side effects.

With regards to the results surrounding the most frequently prescribed medication classes in the current study, stimulants, antidepressants, and atypical antipsychotics were the most frequently prescribed agents in 2001, respectively. In 2009, atypical antipsychotics, stimulants, and alpha-2 agonist agents were the most frequently prescribed medication classes. These most recent findings from 2009 more closely align with the research evidence regarding the safest and most efficacious psychotropic agents (i.e., risperidone, aripiprazole, methylphenidate) used for treating the behaviors associated with autism spectrum disorder. While this is a positive finding, individual characteristics beyond the scope of medical best practice have been found to influence psychopharmacological prescribing practices in the state of Michigan.

Limitations

There are several potential factors that may have influenced the findings surrounding demographic characteristics and the lack of effects on psychopharmacological prescribing practices. First, there may not have been enough variance with regards to demographic

characteristic variables, such as median household income, in order to capture a significant relationship between these characteristics and psychotropic prescribing practices given that this study focused on low-income, Medicaid-enrolled youth. Second, investigations of county-level healthcare characteristics were limited to pediatricians and pediatric specialists who registered with healthychildren.org through the American Academy of Pediatrics. Pediatricians and pediatricians who were not enrolled in this organization could not be accounted for within the current study. Third, analyzing group membership by quartiles for each county demographic characteristic was utilized in order to be consistent with previous research investigating county-level characteristics. Treatment of each characteristic as a continuous variable in order to increase the variance of each predictor may lead to different results within future research. In the setting of the aforementioned limitations, further research is needed in this area before implications of county-level demographics are determined.

From a statistical perspective, an additional limitation includes the potential correlation between county-level independent variables. Overlap in predictor variables due to this correlation with regards to the variance explained may have influenced the insignificant results within statistical analysis of county-level demographic characteristics. Utilization of principal component analysis in order to for each variable to be treated as orthogonal may be a useful method for future research when investigating the effect of county-level variables on psychopharmacological prescribing practices.

In addition to these limitations, a further limitation within this study is the exclusive focus on low-income, Medicaid-enrolled youth. As such, the findings within the current study may not be generalizable to more general populations of youth with autism spectrum disorder. Another limitation within the current study includes the utilization of data through the Center for

Medicare and Medicaid Services. First, the data allows for potential for inconsistent recording of diagnoses and comorbidities if they are subject to varying payment rules. Second, researchers are unable to interpret the reason prescriptions are prescribed within the data set. Lastly, services that have low reimbursement rates may not be included within billings even when services were provided.

In this regard, potential considerations behind the findings within the current study are economic and political influences that may have contributed to the research samples utilized within the current study. More specifically, expansions in Medicaid services to better serve low-income youth in the study have occurred since the year 2000. However, results of the data analysis suggested that the 2001 sample exceeded that of the 2009 sample, which is contraindicated given the expansion in Medicaid services. The resulting sample sizes may have been influenced by documented economic recessions within the state in 2001 and 2008, which may have led to changes in Medicaid-enrollment for Michigan youth.

Implications for Future Research

There are several implications for future research based on the results of the current study. The high prevalence of use of atypical antipsychotics calls for further advances in the research surrounding use of this medication class within youth with autism spectrum disorder, including the safety and efficacy of longer-term use as well as comparative studies of risperidone versus aripiprazole. The high prevalence rates of polypharmacy intervention identified also suggests the need for additional research to identify the neurobiological and clinical implications of use of multiple, concurrent psychotropic medications in developing children with autism spectrum disorder.

In addition, given that the sample within this research study focused exclusively on Medicaid-enrolled youth, differences in prescribing practices between this population and more affluent populations may yield informative data with regards to the effect of socioeconomic status on medication management of the symptoms of autism spectrum disorder. Furthermore, due to the significant changes in psychopharmacological prevalence over the target decade observed within the present study, ongoing evaluation of psychopharmacological prescribing practices may be warranted in order to continue to understand change over time with regards to the treatment of autism spectrum disorder.

A substantive contribution of the current study includes the influence of individual patient characteristics on psychopharmacological treatment practices in the state of Michigan. Research highlighting demographic groups with autism spectrum disorder that are potentially under-identified or underserved would allow future research endeavors to develop specific programming designed to target underserved populations and link families to different modalities of treatment. Moreover, geographical interventions could also be put into place in order to better treat underserved populations with autism spectrum disorder in order to ensure all youth with autism spectrum disorder have the opportunity to access comprehensive treatment practices.

Finally, because behavioral interventions have been identified as the gold standard intervention for addressing the core behavioral symptoms associated with autism spectrum disorder (McDougle, 1997), further research attention should be paid to the influence of utilization of medication management of symptoms on family pursuit of behavioral intervention, such as applied behavior analysis. Analysis of behavioral and medical intervention utilization within the treatment of the behaviors associated with autism spectrum disorder would be a valuable contribution to the research literature.

Conclusions

In summary, prevalence rates of psychopharmacologic prescribing and polypharmacy intervention exceeded previous research findings for youth with autism spectrum disorder within the current study, with prevalence rates increasing dramatically between 2001 and 2009. While advancements in the evidence base regarding the safety and efficacy of psychopharmacologic interventions were mirrored within the research results with regards to the safest and most efficacious medication classes, variables outside of the scope of medical best practice, including age, gender, race, specific diagnostic characteristics, and county education characteristics, have been found to influence the likelihood that youth receive psychopharmacological intervention, As a result, targeted service outreach to underserved populations are warranted in order to ensure all youth with autism spectrum are provided with comprehensive evidence-based treatment within the state of Michigan.

APPENDICES

APPENDIX A: Psychopharmacology Overview

Table 1. *Symptoms Associated with Autism Spectrum Disorder Targeted for Psychopharmacological Intervention*

Target Symptom	Agent	Class
Aggression, Irritability, Self-Injury	*Risperidone	Atypical Antipsychotic
	*Aripiprazole	Atypical Antipsychotic
	Haloperidol	Atypical Antipsychotic
	Methylphenidate	Stimulant
	Divalproex Sodium	Anticonvulsant
	Naltrexone	Opioid Receptor Antagonist
	Clonidine	α2-Adrenergic Agonist
Repetitive Behaviors	*Risperidone	Atypical Antipsychotic
	*Aripiprazole	Atypical Antipsychotic
	Fluoxetine	Antidepressant (SSRI)
	Divalproex Sodium	Anticonvulsant
Hyperactivity	*Risperidone	Atypical Antipsychotic
	*Aripiprazole	Atypical Antipsychotic
	Methylphenidate	Stimulant
	Atomoxetine	Antidepressant (SNRI)
	Clonidine	α2-Agonist
	Guanfacine	α2A-Adrenergic Agonist

*Agents recognized as having the most favorable outcomes per target symptom area when considering behavioral outcomes in conjunction with associated side effects. SSRI: Selective Serotonin Reuptake Inhibitor. SNRI: Selective Norepinephrine Reuptake Inhibitor.

Table 2. *Common Names for Psychotropic Agents by Drug Class (Siegel & Beaulieu, 2012)*

Class	Generic Name	Brand Name
Antipsychotics	Aripiprazole	Abilify
	Chlorpromazine	Thorazine
	Clozapine	Clozaril
	Haloperidol	Haldol
	Olanzapine	Zyprexa
	Perphenazine	Trilafon
	Risperidone	Risperdal
	Ziprasidone	Geodon
SSRIs	Citalopram	Celexa
	Clomipramine	Anafranil
	Desipramine	Norpramin
	Fluoxetine	Prozac
	Fluvoxamine	Luvox
	Paroxetine	Paxil
	Sertraline	Zoloft
Mood Stabilizers	Carbemazepine	Tegretol
	Divalproex	Depakote
	Lamotrigine	Lamictal
	Levetiracetam	Keppra
	Lithium	_
Stimulants	Methylphenidate	Ritalin
	Amphetamine	Adderall
SNRIs	Atomoxetine HCI	Strattera
α-2 Agonists	Clonidine	Catapres
	Guanfacine	Tenex

*SSRI: Selective Serotonin Reuptake Inhibitor. SNRI: Selective Norepinephrine Reuptake Inhibitor.

APPENDIX B: Randomized Controlled Trials per Psychopharmacological Agent

Table 3. *Randomized Controlled Trials of Atypical Antipsychotics for Individuals with Autism Spectrum Disorder*

Agent	Study	Target Symptoms	Dose	Demographics	Side Effects	Positive Outcome(s)
Risperidone	Research Units on Pediatric Psychopharmacology Autism Network, 2002	Irritability, social withdrawal, stereotypy, hyperactivity, inappropriate speech	0.5-3.5 mg/day	101 children and adolescents, Ages 5-17	Weight gain, increased appetite, fatigue, drowsiness, dizziness, drooling, tremor	Significant improvement over placebo in irritability, stereotypy, and hyperactivity
	Research Units on Pediatric Psychopharmacology Autism Network, 2005	Irritability, social withdrawal, stereotypy, hyperactivity, inappropriate speech	0.02-0.06 mg/day	79 children, Ages 5-12	Somnolence, weight gain	Significant improvement over placebo in irritability and hyperactivity
	McDougle et al., 2005	Social interaction, communication, repetitive and stereotyped patterns of behavior	0.5-3.5 mg/day	101 children and adolescents, Ages 5-17	Weight gain, increased appetite, fatigue, drowsiness, dizziness, drooling, tremor, constipation	Significant decreases for sensory motor behaviors, affectual reactions, and sensory responses
Aripiprazole	Owen et al., 2009	Irritability, social withdrawal, stereotypy, hyperactivity, inappropriate speech	5, 10 or 15 mg/day (Flexible dose)	98 children and adolescents Ages 6-17	Fatigue, somnolence, vomiting, sedation	Significant improvement in irritability, hyperactivity, stereotypy, and inappropriate speech.

Table 3 (cont'd).

	Marcus et al., 2009	Irritability, social withdrawal, stereotypy, hyperactivity, inappropriate speech	5, 10, or 15 mg/day (Fixed Dose)	218 children and adolescents Ages 6-17	Sedation, drooling, tremor	Significant improvement over placebo in irritability, stereotypy, hyperactivity, and inappropriate speech

Table 4. *Randomized Controlled Trials of Antidepressants for Individuals with Autism Spectrum Disorder*

Agent	Study	Target Symptoms	Dose	Demographics	Side Effects	Positive Outcome(s)
Fluvoxamine	McDougle et al., 1996	Repetitive Behavior, Disruptive Behavior	50-300 mg/day	15 adults	Mild sedation, gastrointestinal distress	Significant reductions in repetitive behaviors, maladaptive behavior, and aggression
	Sugie et al., 2005	Behavioral Symptoms	1-4 mg/day	18 children Ages 3-8	Transient nausea, hyperactivity	Global improvement in autistic behaviors
Fluoxetine	Buchsbaum et al., 2001	Obsessions	10-40 mg/day	6 adults	Not reported	Reductions in obsessive behaviors
	Hollander et al., 2005	Repetitive Behavior	2.4-20 mg/day	39 children and adolescents Ages 5-17	None reached significance	Significant reductions in repetitive behavior
Citalopram	King et al., 2009	Repetitive Behavior	2.5-20 mg/day	149 children and adolescents Ages 5-17	Hyperactivity, insomnia, inattention, impulsivity, diarrhea	No significant effects on repetitive behavior
Clomipramine	Gordon et al., 1993	Stereotypy, repetitive behavior, compulsions	25-250 mg/day	12 children and adolescents Ages 6-18	Insomnia, constipation, twitching, tremor	Reductions in repetitive behavior
	Remington et al., 2001	Stereotypy, irritability, hyperactivity	100-150 mg/day		Lethargy, tremors, tachycardia, insomnia, diaphoresis, nausea	No significant effects on stereotypy, irritability, or hyperactivity

Table 5. *Randomized Controlled Trials of Stimulants for Individuals with Autism Spectrum Disorder*

Agent	Study	Target Symptoms	Dose	Demographics	Side Effects	Positive Outcome(s)
Methylphenidate	Quintana et al., 1995	Hyperactivity	10-20 mg/day	10 children Ages 7-11	Lack of appetite, insomnia, headache, irritability, stomach ache	Significant reductions in hyperactivity
	Handen et al., 2000	Hyperactivity	0.3-0.6 mg/day	13 children Ages 5-11	Social withdrawal, dullness, sadness, and irritability.	Reductions in hyperactivity, stereotypy, and inappropriate speech
	RUPP, 2005b	Hyperactivity	7.5-50 mg/day	72 children and adolescents Ages 5-14	Appetite decrease, difficulty falling asleep, stomach ache, irritability, emotional outburst	Significant reductions in hyperactivity

Table 6. *Randomized Controlled Trials of Norepinephrine Reuptake Inhibitors and Alpha-2 Adrenergic for Individuals with Autism Spectrum Disorder*

Norepinephrine Reuptake Inhibitors						
Agent	Study	Target Symptoms	Dose	Demographics	Side Effects	Positive Outcome(s)
Atomoxetine	Arnold et al., 2006	Hyperactivity, Inattention	0.25-1.4 mg/day	16 children and adolescents Ages 5-15	Restlessness, irritability, fatigue, insomnia, decreased appetite, upset stomach	Significant reduction in hyperactivity
Alpha-2 Adrenergic Agonists						
Agent	Study	Target Symptoms	Dose	Demographics	Side Effects	Positive Outcome(s)
Clonidine	Fankhauser et al., 1992	Hyperactivity, irritability, inappropriate speech, stereotypy	0.15-0.20 mg	8 children 5-13 years old	Drowsiness, hypotension	Significant decrease in irritability
	Jaselskis et al., 1992	Hyperactivity, irritability, inappropriate speech, stereotypy	0.15-0.20 mg	8 children	Drowsiness, fatigue	Significant decrease in hyperactivity

Table 7. *Randomized Controlled Trials of Anticonvulsants for Individuals with Autism Spectrum Disorder*

Agent	Study	Target Symptoms	Dose	Demographics	Side Effects	Positive Outcome(s)
Lamotrigine	Belsito et al., 2001	Stereotypies, lethargy, irritability, hyperactivity, emotional reciprocity, sharing pleasures	5.0 mg/kg/day	28 children Ages 3-11	Insomnia, hyperactivity	No significant benefits over placebo
Levitiracetam	Wasserman et al., 2006	Irritability, global functioning	20-30 mg/kg/day	20 children Ages 5-17	Aggression	No significant benefits for irritability or global functioning
Valproate	Hellings et al., 2005	Irritability	20 mg/kg/day	30 children and adolescents Ages 6-20	Increased appetite, skin rash	No significant benefits on irritability
Divalproex Sodium	Hollander et al., 2006	Repetitive behavior	500-1,500 mg/day	12 children Ages 5-17	Irritability, aggression	Significant decrease in repetitive behavior

APPENDIX C: Psychopharmacological Agents for Youth with Autism Spectrum Disorder

Table 8. *Most Commonly Prescribed Agents for Youth with Autism Spectrum Disorder by Class*

Aman et al.1995						
Antipsychotics	Antidepressants	Mood Stabilizers	Stimulants	Sedatives/Anxiolytics/	Antihypertensives	Anticonvulsants
Thioridazine	Clomipramine	Lithium	Methylphenidate	Chloral Hydrate	Clonidine	Carbemazepine
Haloperidol	Imipramine	Carbemazepine	Dextroamphetamine	Buspirone	Propranolol	Valproic Acid
Chlorpromazine	Fluoxetine	Clonazepam	Pemoline	Hydroxyzine		Phenytoin
Langworthy-Lam et al. 2002						
Antipsychotics	Antidepressants	Mood Stabilizers	Stimulants	Sedatives/Anxiolytics	Antihypertensives	Anticonvulsants
Risperidone	Fluoxetine	Valproic Acid	Methylphenidate	Melatonin	Clonidine	Carbemazepine
Olanzapine	Sertraline	Carbemazepine	Dextroamphetamine	Buspirone	Guanfacine	Valproic Acid
Thioridazine	Paroxetine	Lithium		Lorazepam	Propranolol	Gabapentin
Aman et al. 2003						
Antipsychotics	Antidepressants	Mood Stabilizers	Stimulants	Sedatives/Anxiolytics	Antihypertensives	Anticonvulsants
Risperidone	Fluoxetine	Valproic Acid	Methylphenidate	Melatonin	Clonidine	Valproic Acid
Olanzapine	Sertraline	Carbemazepine	Dextroamphetamine	Buspirone	Propranolol	Carbemazepine
Thioridazine	Fluvoxamine	Lithium	Amphetamine Salts	Diazepam	Metoprolol	Lamotrigine

Note: Information included from all studies reporting most commonly prescribed agents according to medication class within the target population.

APPENDIX D: Statistical Outcomes

Table 9. *Psychotropic Prevalence Rates for Youth with Autism Spectrum Disorder*

	Aman et al. 1995	Langworthy et al. 2002	Aman et al. 2003	Mandell et al. 2008
Neuroleptics	12.2%	16.8%	14.9%	31.0%
Antidepressants	6.1%	21.7%	21.6%	25.0%
Stimulants	6.6%	13.9%	11.3%	22.0%
Antihypertensives	4.4%	9.5%	12.5%	_
Mood Stabilizers	3.9%	5.1%	4.5%	21.0%
Anxiolytics/Sedatives	6.3%	7.3%	_	_
Anticonvulsants	_	12.4%	11.5%	_

Table 10. *Descriptive Statistics for Independent Variables (Predictors) – 2009 Data Set*

	N	%
Sample Size	2967	-
Autistic Disorder	2343	79.0
Asperger's Disorder	596	20.1
Unspecified Pervasive Developmental Disorder	28	0.9
Presence of Comorbidity	1221	41.2
Ages 0-5	590	19.9
Ages 6-12	1792	60.4
Ages 13-17	585	19.7
Male	2392	80.6
Female	575	19.4
White	1845	62.2
Black	612	20.6
American Indian/Alaskan	21	0.7
Asian	18	0.6
Hawaiian/Pacific Islander	59	2.0
Other	412	13.9
Mental Retardation	550	18.5
Mood Disorders	255	8.6
Communication/Developmental Disorder	244	8.2
Attention-Deficit/Hyperactivity Disorder	248	8.4
Disruptive Behavior Disorder	115	3.9
Anxiety Disorder	72	2.4

Table 11. *Number of Insurance Claims per Type of Medicaid Analytic Extract (MAX) File by Year*

MAX File Type	2001	2009	Total
Personal Summary	5,210	7,252	12,462
Prescription Drug	30,899	119,991	150,890
Inpatient	148	285	433
Long Term Care	111	1,142	1,253
Other Therapy	263,265	829,250	1,092,515

Table 12. *Prevalence Rates of Psychopharmacologic Prescribing by Individual Participant Characteristics*

Parameter	% Prescribed Psychotropic Medication	% Polypharmacy	Atypical Antipsychotic	Stimulant	Antidepressant	Antiadrenergic	Anticonvulsant	Antipsychotic	Miscellaneous Anxiolytics, Sedatives, and Hynpotics
Autistic Disorder (N = 2343)	58.6	35.2	32.9	31.7	18.9	20.2	18.0	4.7	8.5
Asperger's Disorder (N = 596)	66.1	40.4	38.4	37.9	22.5	20.5	21.3	7.7	7.9
Ages 0-5 (N = 590)	37.6	11.9	16.3	9.0	3.6	14.7	8.1	0.3	10.7
Ages 6-12 (N = 1792)	63.3	39.1	36.6	39.3	19.5	22.7	18.2	4.5	7.5
Ages 13-17 (N = 585)	72.8	52.3	43.9	36.9	36.4	18.6	31.3	13.8	9.2
Gender - Male (N = 2392)	60.5	36.2	34.7	34.7	19.4	21.3	18.1	5.4	8.1
Gender - Female (N = 575)	58.1	36.5	31.1	25.2	21	16.0	21.9	5.7	9.9
Race - White (N = 1845)	65.7	42.4	38.2	38.0	23.8	23.3	21.8	6.3	8.6
Race - Black (N = 612)	52.1	26.6	29.4	24	10.1	16.0	15.1	5.1	8.5
Race - American Indian/Alaskan (N = 21)	71.4	28.6	14.3	52.4	42.9	0.0	14.3	0.0	4.8
Race - Asian (N = 18)	61.1	33.3	16.7	27.8	5.6	22.2	22.2	11.1	11.1
Race - Hawaiian/Pacific Islander (N = 59)	47.5	22.0	18.6	20.3	11.9	13.6	15.3	5.1	10.2
Comorbidity (N = 1221)	62.7	41.6	37.8	33.6	23.3	22.9	23	7.4	8.8
No Comorbidity (N = 1746)	58.2	32.5	31.4	32.3	17.1	18.5	15.9	4.2	8.2

Table 13. *Logistic Regression Predicting Presence of Psychotropic Prescription*

Parameter	Odds Ratio (95% CI)	P
Autism Spectrum Diagnosis *(Reference is Asperger's Disorder)*		
Autistic Disorder	0.751 (0.624-0.903)	0.002*
Age *(Reference Category is 0- to 5-year-olds)*		
6- to 12-year-olds	2.857 (2.357-3.462)	0.000*
13- to 17-year-olds	4.441 (3.470-5.685)	0.000*
Gender *(Reference Category is Male)*		
Female	0.904 (0.751-1.087)	0.282
Race *(Reference Category is White)*		
Black	0.655 (0.547-0.784)	0.000*
American Indian/Alaskan	1.505 (0.582-3.893)	0.400
Asian	0.946 (0.365-2.449)	0.909
Hawaiian/Pacific Islander	0.544 (0.324-0.913)	0.021
Comorbid Diagnoses		
Presence of Comorbidity	1.203 (1.035-1.397)	0.016
Total Student Expenditures *(Reference category is lowest percentile)*		
Quartile 2	1.119 (0.949-1.319)	0.181
Quartile 3	0.818 (0.652-1.026)	0.082
Quartile 4	0.965 (0.686-1.359)	0.839
Proportion of Students in Special Education *(Reference category is lowest percentile)*		
Quartile 2	0.946 (0.798-1.121)	0.520
Quartile 3	0.762 (0.604-0.961)	0.022
Quartile 4	0.965 (0.754-1.234)	0.774
Total Number of Students *(Reference category is lowest percentile)*		
Quartile 2	1.307 (1.106-1.544)	0.002*
Quartile 3	1.267 (0.952-1.688)	0.105
Quartile 4	0.899 (0.714-1.132)	0.364
Pupil/Teacher Ratio *(Reference category is lowest percentile)*		
Quartile 2	1.002 (0.852-1.178)	0.981
Quartile 3	0.761 (0.605-0.957)	0.020
Quartile 4	0.685 (0.457-1.027)	0.067
Number Pediatricians/Pediatric Specialists *(Reference category is lowest percentile)*		
Quartile 2	1.008 (0.746-1.364)	0.956
Quartile 3	1.017 (0.859-1.205)	0.841
Quartile 4	0.954 (0.771-1.181)	0.665
Median Household Income *(Reference category is lowest percentile)*		
Quartile 2	0.886 (0.678-1.158)	0.377
Quartile 3	0.890 (0.673-1.178)	0.415
Quartile 4	0.928 (0.722-1.193)	0.562
Percentage White Residents *(Reference category is lowest percentile)*		
Quartile 2	1.148 (0.944-1.397)	0.167
Quartile 3	0.911 (0.729-1.137)	0.410
Quartile 4	1.036 (0.841-1.276)	0.740
Percentage Living in Poverty *(Reference category is lowest percentile)*		
Quartile 2	1.174 (0.979-1.406)	0.083
Quartile 3	1.015 (0.848-1.214)	0.873
Quartile 4	1.536 (0.722-3.269)	0.265
Percentage Medicaid-Enrolled Youth *(Reference category is lowest percentile)*		
Quartile 2	0.978 (0.696-1.374)	0.899
Quartile 3	1.003 (0.714-1.409)	0.985
Quartile 4	1.041 (0.750-1.444)	0.810

**Note. (*) represents independent variables significant at the $p \leq 0.004$ per Bonferroni adjustment.*

Table 14. *Logistic Regression Predicting Presence of Polypharmacy*

Parameter	Odds Ratio (95% CI)	P
Autism Spectrum Diagnosis *(Reference category is Asperger's disorder)*		
Autistic Disorder	0.801 (0.668-0.960)	0.016
Age *(Reference category is 0- to 5-year-olds)*		
6- to 12-year-olds	4.762 (3.646-6.219)	0.000*
13- to 18-year-olds	8.147 (6.050-10.972)	0.000*
Gender *(Reference Category is male)*		
Female	1.014 (0.839-1.225)	0.887
Race *(Reference category is White)*		
Black	0.560 (0.459-0.682)	0.000*
American Indian/Alaskan	0.617 (0.238-1.595)	0.319
Asian	0.771 (0.288-2.061)	0.604
Hawaiian/Pacific Islander	0.436 (0.234-0.811)	0.009
Comorbid Diagnoses *(Reference category is absence of comorbidity)*		
Presence of Comorbidity	1.478 (1.270-1.719)	0.000*
Total Student Expenditures *(Reference category is lowest percentile)*		
Quartile 2	1.071 (0.907-1.265)	0.416
Quartile 3	0.878 (0.692-1.114)	0.283
Quartile 4	1.047 (0.739-1.483)	0.796
Proportion of Students in Special Education *(Reference category is lowest percentile)*		
Quartile 2	0.961 (0.809-1.141)	0.651
Quartile 3	0.825 (0.648-1.051)	0.119
Quartile 4	0.835 (0.648-1.076)	0.164
Total Number of Students *(Reference category is lowest percentile)*		
Quartile 2	1.217 (1.029-1.440)	0.022
Quartile 3	1.128 (0.846-1.505)	0.411
Quartile 4	0.947 (0.743-1.207)	0.661
Pupil/Teacher Ratio *(Reference category is lowest percentile)*		
Quartile 2	0.965 (0.820-1.136)	0.668
Quartile 3	0.826 (0.649-1.049)	0.117
Quartile 4	0.630 (0.401-0.987)	0.044
Number Pediatricians/Pediatric Specialists *(Reference category is lowest percentile)*		
Quartile 2	1.160 (0.856-1.570)	0.338
Quartile 3	1.077 (0.907-1.279)	0.399
Quartile 4	0.924 (0.741-1.152)	0.483
Median Household Income *(Reference category is lowest percentile)*		
Quartile 2	0.937 (0.716-1.226)	0.636
Quartile 3	0.861 (0.649-1.142)	0.299
Quartile 4	0.919 (0.715-1.182)	0.510
Percentage White Residents *(Reference category is lowest percentile)*		
Quartile 2	1.035 (0.849-1.261)	0.735
Quartile 3	0.861 (0.684-1.084)	0.203
Quartile 4	0.995 (0.805-1.230)	0.995
Percentage Living in Poverty *(Reference category is lowest percentile)*		
Quartile 2	1.068 (0.889-1.282)	0.482
Quartile 3	1.051 (0.875-1.263)	0.595
Quartile 4	1.242 (0.608-2.535)	0.552
Percentage Medicaid-Enrolled Youth *(Reference category is lowest percentile)*		
Quartile 2	1.052 (0.743-1.490)	0.775
Quartile 3	1.050 (0.742-1.487)	0.782
Quartile 4	1.017 (0.728-1.423)	0.920

**Note. (*) represents independent variables significant at the $p \leq 0.004$ per Bonferroni adjustment.*

Table 15. *Negative Binomial Regression Predicting Total Number of Psychopharmacologic Prescriptions*

Parameter	B	S.E.	Wald Chi-Square	df	Sig.
Autistic Disorder *(Reference Category: Asperger's Disorder)*	0.012	0.049	0.064	1	0.800
Age - 6- to 12-year-olds *(Reference Category: 0- to 5-year-olds)*	1.313	0.055	574.616	1	0.000*
Age - 13- to 18-year-olds *(Reference Category: 0- to 5-year-olds)*	1.672	0.066	649.211	1	0.000*
Gender - Female *(Reference Category: Male)*	-0.022	0.050	0.194	1	0.660
Race - Black *(Reference Category: White)*	-0.278	0.050	31.422	1	0.000*
Race American Indian/Alaskan *(Reference Category: White)*	-0.569	0.237	5.779	1	0.016
Race - Asian *(Reference Category: White)*	-0.376	0.253	2.222	1	0.136
Race - Hawaiian/Pacific Islander *(Reference Category: White)*	-0.722	1.457	24.543	1	0.000*
Comorbidity *(Reference Category: No Comorbidity)*	0.170	0.040	18.103	1	0.000*
Total Student Expenditures - Quartile 2	0.099	0.049	4.122	1	0.042
Total Student Expenditures - Quartile 3	-0.106	0.363	0.085	1	0.770
Total Student Expenditures - Quartile 4	0.062	0.093	0.441	1	0.506
Proportion in Special Education - Quartile 2	-0.038	0.047	0.647	1	0.421
Proportion in Special Education - Quartile 3	-0.212	0.359	0.348	1	0.555
Proportion in Special Education - Quartile 4	-0.172	0.070	5.990	1	0.014
Total Number of Students - Quartile 2	0.105	0.052	4.083	1	0.043
Total Number of Students - Quartile 3	0.093	0.086	1.180	1	0.277
Total Number of Students - Quartile 4	-0.091	0.091	1.016	1	0.314
Pupil/Teacher Ratio - Quartile 2	-0.064	0.047	1.834	1	0.176
Pupil/Teacher Ratio - Quartile 3	-0.243	0.320	0.576	1	0.448
Pupil/Teacher Ratio - Quartile 4	-0.458	0.128	12.877	1	0.000*
Pediatricians/Pediatric Specialists - Quartile 2	-0.087	0.084	1.059	1	0.303
Pediatricians/Pediatric Specialists - Quartile 3	-0.051	0.050	1.014	1	0.314
Pediatricians/Pediatric Specialists - Quartile 4	-0.102	0.065	2.494	1	0.114
Median Household Income - Quartile 2	0.007	0.146	0.002	1	0.962
Median Household Income - Quartile 3	-0.108	0.085	1.619	1	0.203
Median Household Income - Quartile 4	-0.071	0.093	0.586	1	0.444
Percentage White Residents - Quartile 2	-0.063	0.088	0.512	1	0.474
Percentage White Residents - Quartile 3	-0.037	0.106	0.123	1	0.725
Percentage White Residents - Quartile 4	0.044	0.114	0.153	1	0.696
Percentage Living in Poverty - Quartile 2	0.102	0.072	1.997	1	0.158
Percentage Living in Poverty - Quartile 3	0.270	0.154	3.065	1	0.080
Percentage Living in Poverty - Quartile 4	-0.026	0.205	0.016	1	0.901
Percentage Medicaid-Enrolled - Quartile 2	0.160	0.130	1.515	1	0.218
Percentage Medicaid-Enrolled - Quartile 3	0.068	0.095	0.518	1	0.472
Percentage Medicaid-Enrolled - Quartile 4	0.062	0.092	0.456	1	0.500

Table 16. *Negative Binomial Regression Predicting Total Number of Psychotropic Agents*

Parameter	B	S.E.	Wald Chi-Square	df	Sig.
Autistic Disorder *(Reference Category: Asperger's Disorder)*	-0.031	0.0573	0.299	1	0.584
Age - 6- to 12-year-olds *(Reference Category: 0- to 5-year-olds)*	0.906	0.0703	166.350	1	0.000*
Age - 13- to 18-year-olds *(Reference Category: 0- to 5-year-olds)*	1.114	0.0820	184.696	1	0.000*
Gender - Female *(Reference Category: Male)*	-0.018	0.0596	0.087	1	0.768
Race - Black *(Reference Category: White)*	-0.270	0.0609	19.679	1	0.000*
Race American Indian/Alaskan *(Reference Category: White)*	-0.335	0.2847	1.388	1	0.239
Race - Asian *(Reference Category: White)*	-0.303	0.3132	0.939	1	0.333
Race - Hawaiian/Pacific Islander *(Reference Category: White)*	-0.487	0.1835	0.706	1	0.008
Comorbidity *(Reference Category: No Comorbidity)*	0.192	0.0478	16.143	1	0.000*
Total Student Expenditures - Quartile 2	0.083	0.0587	2.017	1	0.156
Total Student Expenditures - Quartile 3	-0.297	0.4122	0.518	1	0.472
Total Student Expenditures - Quartile 4	-0.007	0.1118	0.004	1	0.947
Proportion in Special Education - Quartile 2	-0.058	0.0562	1.065	1	0.302
Proportion in Special Education - Quartile 3	-0.388	0.4208	0.849	1	0.357
Proportion in Special Education - Quartile 4	-0.135	0.0850	2.513	1	0.113
Total Number of Students - Quartile 2	0.083	0.0620	1.786	1	0.181
Total Number of Students - Quartile 3	0.098	0.1033	0.903	1	0.342
Total Number of Students - Quartile 4	-0.086	0.1097	0.621	1	0.431
Pupil/Teacher Ratio - Quartile 2	-0.072	0.0561	1.653	1	0.199
Pupil/Teacher Ratio - Quartile 3	-0.348	0.3673	0.897	1	0.344
Pupil/Teacher Ratio - Quartile 4	-0.439	0.1588	7.635	1	0.006
Pediatricians/Pediatric Specialists - Quartile 2	-0.077	0.1023	0.560	1	0.454
Pediatricians/Pediatric Specialists - Quartile 3	-0.020	0.0600	0.115	1	0.735
Pediatricians/Pediatric Specialists - Quartile 4	-0.016	0.0773	0.042	1	0.837
Median Household Income - Quartile 2	-0.115	0.1713	0.447	1	0.504
Median Household Income - Quartile 3	-0.182	0.0996	3.342	1	0.068
Median Household Income - Quartile 4	-0.078	0.1105	0.503	1	0.478
Percentage White Residents - Quartile 2	-0.010	0.1031	0.009	1	0.924
Percentage White Residents - Quartile 3	0.000	0.1241	0.000	1	0.999
Percentage White Residents - Quartile 4	0.068	0.1329	0.261	1	0.610
Percentage Living in Poverty - Quartile 2	0.082	0.0855	0.909	1	0.340
Percentage Living in Poverty - Quartile 3	0.213	0.1836	1.340	1	0.247
Percentage Living in Poverty - Quartile 4	0.049	0.2454	0.040	1	0.842
Percentage Medicaid-Enrolled - Quartile 2	0.158	0.1566	1.019	1	0.313
Percentage Medicaid-Enrolled - Quartile 3	0.079	0.1160	0.466	1	0.495
Percentage Medicaid-Enrolled - Quartile 4	0.126	0.1117	1.278	1	0.258

Table 17. *Negative Binomial Regression Predicting Total Number of Medication Classes*

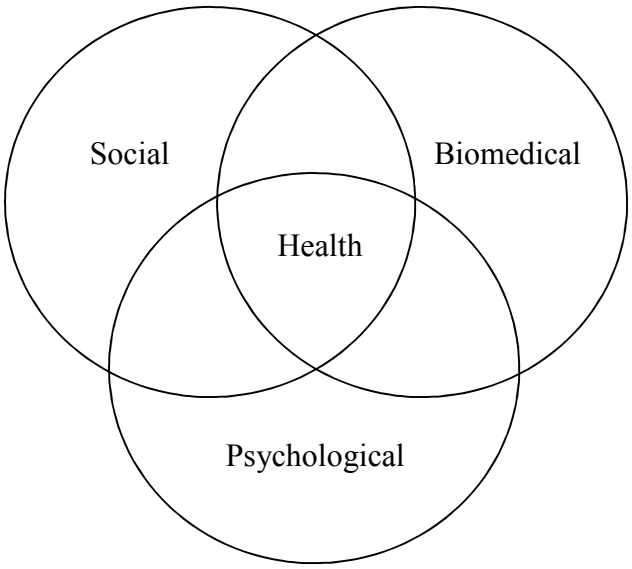
Parameter	B	S.E.	Wald Chi-Square	df	Sig.
Autistic Disorder *(Reference Category: Asperger's Disorder)*	-0.018	0.0599	0.087	1	0.768
Age - 6- to 12-year-olds *(Reference Category: 0- to 5-year-olds)*	0.839	0.0740	128.525	1	0.000*
Age - 13- to 18-year-olds *(Reference Category: 0- to 5-year-olds)*	1.068	0.0859	154.531	1	0.000*
Gender - Female *(Reference Category: Male)*	-0.074	0.0629	1.378	1	0.240
Race - Black *(Reference Category: White)*	-0.278	0.0641	18.786	1	0.000*
Race American Indian/Alaskan *(Reference Category: White)*	-0.282	0.2964	0.902	1	0.342
Race - Asian *(Reference Category: White)*	-0.231	0.3254	0.504	1	0.478
Race - Hawaiian/Pacific Islander *(Reference Category: White)*	-0.454	0.1925	5.552	1	0.018
Comorbidity *(Reference Category: No Comorbidity)*	0.139	0.0502	7.636	1	0.006
Total Student Expenditures - Quartile 2	0.071	0.0614	1.326	1	0.250
Total Student Expenditures - Quartile 3	-0.269	0.4275	0.396	1	0.529
Total Student Expenditures - Quartile 4	-0.024	0.1170	0.041	1	0.839
Proportion in Special Education - Quartile 2	-0.043	0.0587	0.548	1	0.459
Proportion in Special Education - Quartile 3	-0.358	0.4387	0.666	1	0.414
Proportion in Special Education - Quartile 4	-0.114	0.0891	1.625	1	0.202
Total Number of Students - Quartile 2	0.082	0.0646	1.601	1	0.206
Total Number of Students - Quartile 3	0.093	0.1080	0.738	1	0.390
Total Number of Students - Quartile 4	-0.076	0.1138	0.441	1	0.507
Pupil/Teacher Ratio - Quartile 2	-0.083	0.0587	1.989	1	0.158
Pupil/Teacher Ratio - Quartile 3	-0.283	0.3822	0.547	1	0.460
Pupil/Teacher Ratio - Quartile 4	-0.392	0.1658	5.600	1	0.018
Pediatricians/Pediatric Specialists - Quartile 2	-0.070	0.1063	0.431	1	0.512
Pediatricians/Pediatric Specialists - Quartile 3	-0.030	0.0627	0.224	1	0.636
Pediatricians/Pediatric Specialists - Quartile 4	-0.032	0.0809	0.159	1	0.690
Median Household Income - Quartile 2	-0.140	0.1783	0.614	1	0.433
Median Household Income - Quartile 3	-0.184	0.1043	3.102	1	0.078
Median Household Income - Quartile 4	-0.096	0.1161	0.682	1	0.409
Percentage White Residents - Quartile 2	0.002	0.1076	0.000	1	0.989
Percentage White Residents - Quartile 3	-0.015	0.1297	0.013	1	0.908
Percentage White Residents - Quartile 4	0.060	0.1387	0.189	1	0.664
Percentage Living in Poverty - Quartile 2	0.099	0.0895	1.220	1	0.269
Percentage Living in Poverty - Quartile 3	0.212	0.1911	1.228	1	0.268
Percentage Living in Poverty - Quartile 4	0.105	0.2559	0.170	1	0.680
Percentage Medicaid-Enrolled - Quartile 2	0.120	0.1630	0.545	1	0.460
Percentage Medicaid-Enrolled - Quartile 3	0.090	0.1211	0.551	1	0.458
Percentage Medicaid-Enrolled - Quartile 4	0.103	0.1168	0.781	1	0.377

Table 18. *Prevalence Rates of Psychopharmacologic Prescribing by Individual Participant Characteristics*

Parameter	% Prescribed Psychotropic Medication	% Polypharmacy	Atypical Antipsychotic	Stimulant	Antidepressant	Antiadrenergic	Anticonvulsant	Antipsychotic	Miscellaneous Anxiolytics, Sedatives, and Hynpotics
Total Student Expenditures - Q1	59.8	36.0	33.8	31.6	20.0	20.2	19.5	5.8	8.4
Total Student Expenditures - Q2	62.5	37.6	35.5	34.7	21.1	22.0	19.4	5.3	8.6
Total Student Expenditures - Q3	54.9	33.1	30.5	31.0	15.1	15.6	15.1	5.4	8.7
Total Student Expenditures - Q4	58.9	37.1	34.4	35.1	18.5	20.5	17.9	4.6	7.3
% in Special Education - Q1	61.5	37.6	35.9	34.6	20.9	19.8	20.0	5.7	9.3
% in Special Education - Q2	60.2	36.7	32.9	30.8	20.8	22.7	19.6	5.8	7.5
% in Special Education - Q3	54.9	33.2	30.4	31.2	15.2	15.7	15.2	5.4	8.8
% in Special Education - Q4	60.6	33.5	35.0	35.0	17.2	19.8	16.3	3.8	8.2
Total # of Students - Q1	57.5	34.5	31.1	31.1	19.2	20.6	18.3	6.0	7.6
Total # of Students - Q2	63.9	39.0	37.7	35.0	21.9	21.7	20.3	4.7	9.3
Total # of Students - Q3	63.2	37.2	37.2	34.3	19.2	19.7	20.1	6.7	8.4
Total # of Students - Q4	54.9	33.2	30.4	31.2	15.2	15.7	15.2	5.4	8.8
Pupil/Teacher Ratio - Q1	61.2	37.5	35.3	32.9	21	21.1	19.9	5.9	9.0
Pupil/Teacher Ratio - Q2	61.3	36.7	34.1	33.5	20.5	21.4	19.8	5.4	8.2
Pupil/Teacher Ratio - Q3	54.6	33.2	30.4	31.1	15.3	15.6	15.3	5.4	8.9
Pupil/Teacher Ratio - Q4	52.0	27.5	31.4	30.4	10.8	14.7	7.8	2.0	3.9
# Ped/Ped Specialists - Q1	60.1	35.7	32.4	32.1	18.9	21.8	18.7	5.9	9.1
# Ped/Ped Specialists - Q2	60.3	39.2	34.8	37.3	19.6	16.7	18.6	3.9	5.9
# Ped/Ped Specialists - Q3	60.5	37.5	35.5	32.6	21.1	19.5	19.2	5.1	8.7
# Ped/Ped Specialists - Q4	59.0	34.0	35.0	33.3	19.0	19.4	18.3	5.8	7.3
Median Household Income - Q1	62.1	38.2	33.2	34.2	20.2	25.2	17.7	5.3	9.0
Median Household Income - Q2	59.2	36.7	34.6	32.8	19.4	18.7	17.4	5.5	9.6
Median Household Income - Q3	59.3	34.7	33.3	31.1	19.7	18.8	18.5	5.2	7.9
Median Household Income - Q4	60.4	36.2	34.2	33.3	19.7	20.6	20.0	5.6	7.9
% White Residents - Q1	59.2	36.7	34.6	32.8	19.4	18.7	17.4	5.5	9.6
% White Residents - Q2	62.5	37.5	35.7	33.9	21.1	20.2	19.2	5.1	8.8
% White Residents - Q3	57.0	33.3	32.7	31.6	18.1	19.9	16.8	4.9	7.6
% White Residents - Q4	60.1	36.6	32.2	32.4	19.3	22.4	21.3	6.4	7.4
% Living in Poverty - Q1	58.9	35.5	33.3	31.7	19.5	20.9	19.3	5.7	7.6
% Living in Poverty - Q2	62.7	37.0	34.2	34.8	20.8	20.5	19.4	5.1	8.8
% Living in Poverty - Q3	59.2	36.7	34.6	32.8	19.4	18.7	17.4	5.5	9.6
% Living in Poverty - Q4	68.8	40.6	46.9	34.4	9.4	25.0	15.6	3.1	9.4
% Medicaid-Enrolled - Q1	59.8	35.5	32.5	28.4	16	21.9	18.3	4.1	8.3
% Medicaid-Enrolled - Q2	59.2	36.7	34.6	32.8	19.4	18.7	17.4	5.5	9.6
% Medicaid-Enrolled - Q3	59.8	36.6	34.3	32.7	20.9	20.9	19.0	6.3	8.0
% Medicaid-Enrolled - Q4	60.7	35.9	33.7	33.5	19.6	20.7	19.6	5.2	8.1

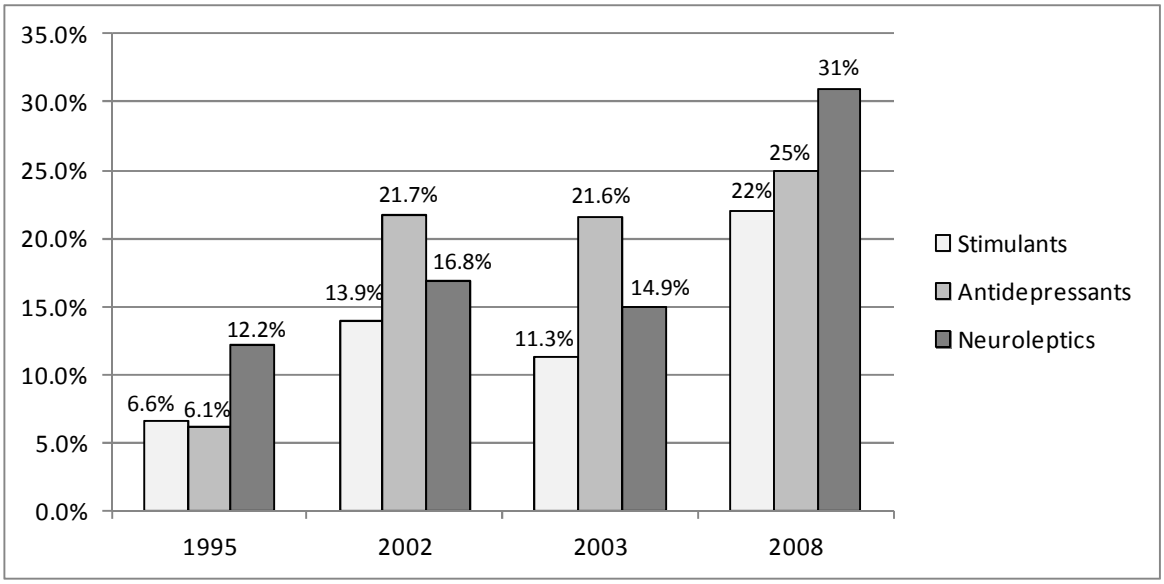
APPENDIX E: Theoretical Perspective

Figure 1. *Biopsychosocial Model of Health Outcomes*



APPENDIX F: Graphical Depiction of Prior Study Results

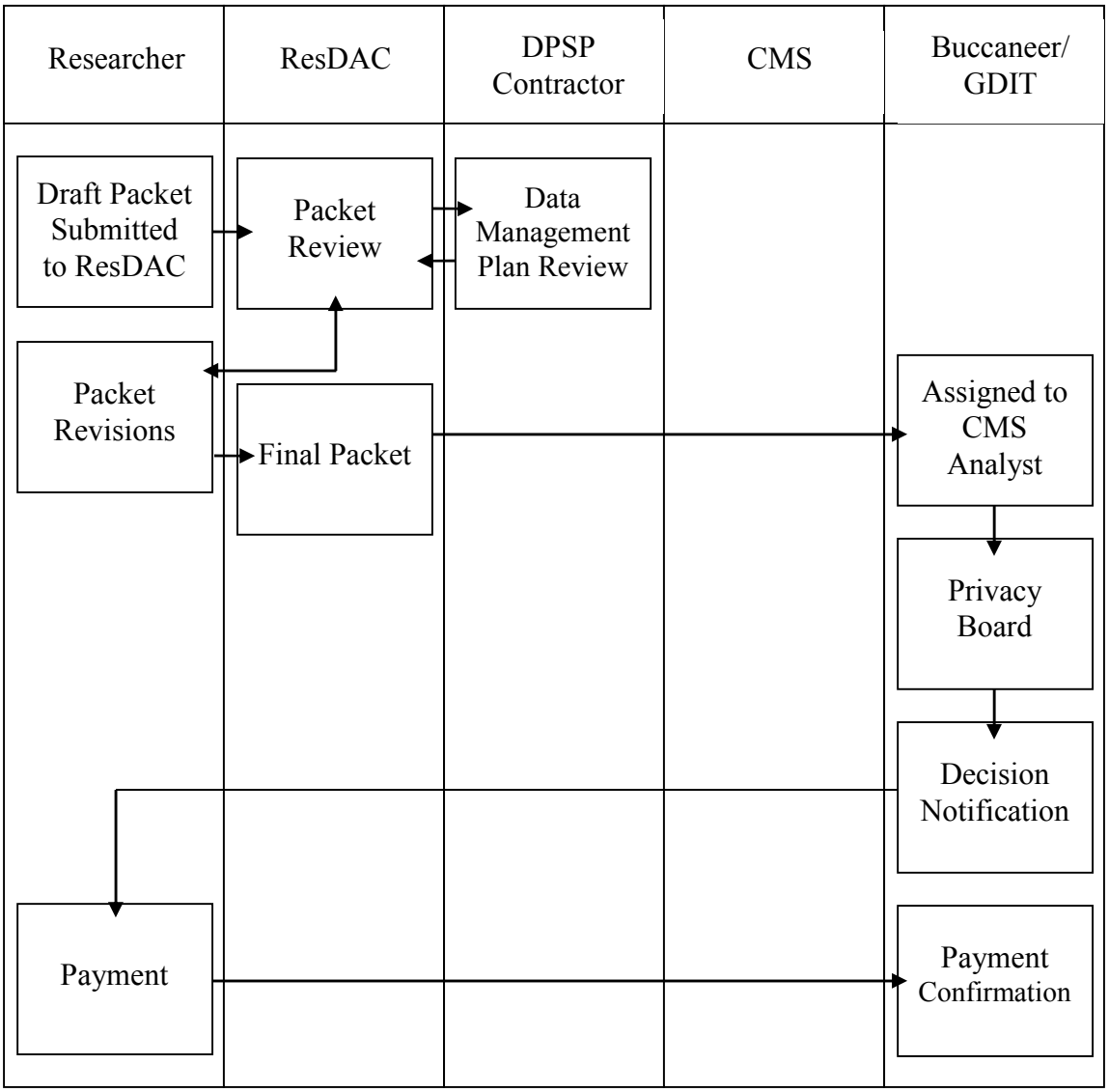
Figure 2. *Increases in the Three Most Common Psychotropic Medications for Youth with Autism Spectrum Disorder*



Note: Statistics above based on data from Aman et al. (1995), Langworthy et al. (2002), Aman et al. (2003), and Mandell et al. (2008). Statistics from Martin et al. (1999) not included due to exclusive focus on Asperger's Disorder.

APPENDIX G: Data Request Process

Figure 3. *Research Data Assistance Center (ResDAC) Data Request Flowchart*



APPENDIX H: Graphical Depictions of Prevalence Rates

Figure 4. *Prevalence of Psychopharmacologic Prescribing Practices for Children and Adolescents Diagnosed with Autism Spectrum Disorder (2009)*

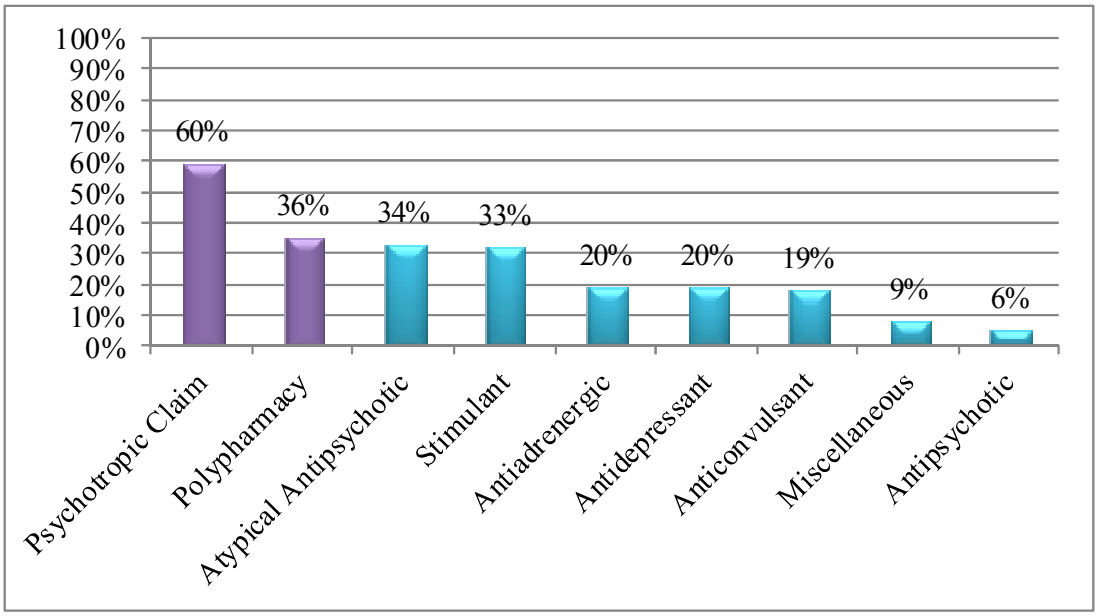
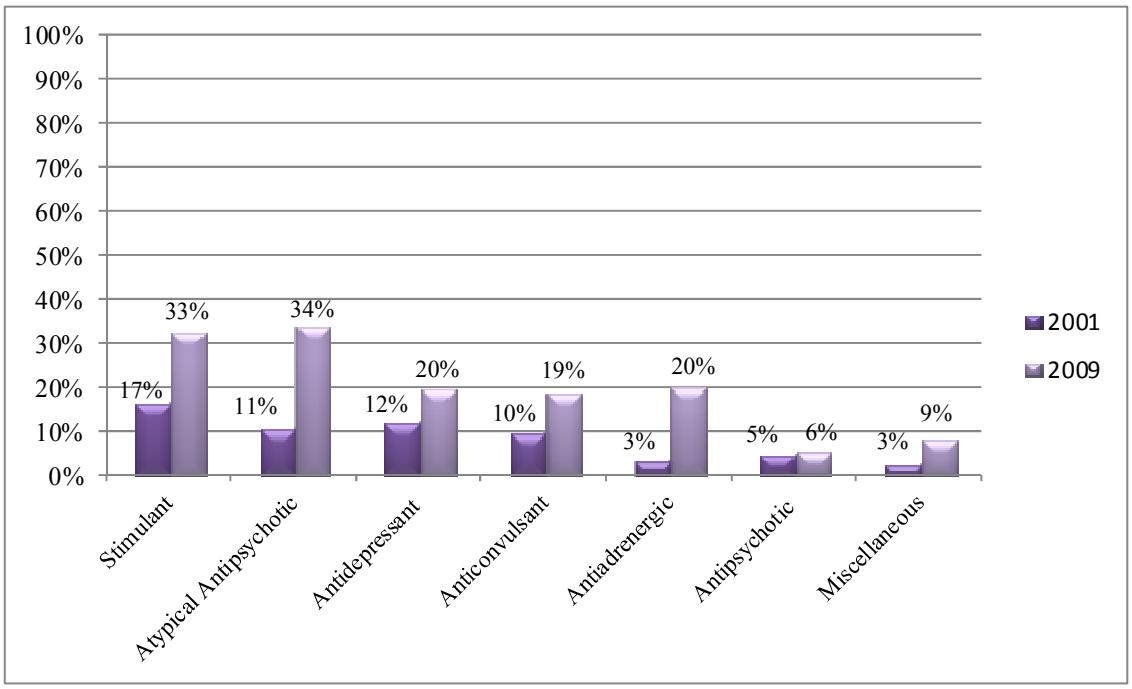


Figure 5. *Changes in Psychopharmacologic Prescribing Practices for Children and Adolescents with Autism Spectrum Disorder according to Medication Class between 2001 and 2009 Year*



APPENDIX I: Medicaid Analytic Extract (MAX) File Variables

Medicaid Analytic Extract (MAX) Personal Summary File Variables

Column	Variable Name	Label
1	BENE_ID	Encrypted 723 CCW Beneficiary ID
2	MSIS_ID	Encrypted MSIS Identification Number
3	STATE_CD	State
4	EL_STATE_CASE_NUM	Encrypted Case Number
5	MAX_YR_DT	Year
6	HGT_FLAG	SSN (from MSIS) High Group Test
7	EXT_SSN_SRCE	External SSN source
8	EL_DOB	Date of birth
9	EL_AGE_GRP_CD	Age group
10	EL_SEX_CD	Sex
11	EL_RACE_ETHNCY_CD	Race/ethnicity (from MSIS)
12	RACE_CODE_1	Race - White (from MSIS)
13	RACE_CODE_2	Race - Black (from MSIS)
14	RACE_CODE_3	Race - Am Indian/Alaskan (from MSIS)
15	RACE_CODE_4	Race - Asian (from MSIS)
16	RACE_CODE_5	Race - Hawaiian/Pac) Islands (from MSIS)
17	ETHNICITY_CODE	Ethnicity - Hispanic (from MSIS)
18	MDCR_RACE_ETHNCY_CD	Race/ethnicity (from Medicare EDB)
19	MDCR_LANG_CD	Language code (from Medicare EDB)
20	EL_SEX_RACE_CD	Sex/race
21	EL_DOD	Date of death (from MSIS)
22	MDCR_DOD	Date of death (from Medicare EDB)
23	MDCR_DEATH_DAY_SW	Day of death verified (from Mcare EDB)
24	EL_RSDNC_CNTY_CD_LTST	County of residence
25	EL_RSDNC_ZIP_CD_LTST	Zip code of residence
26	EL_SS_ELGBLTY_CD_LTST	State specific eligibility - most recent
27	EL_MAX_ELGBLTY_CD_LTST	MAX eligibility - most recent
28	MSNG_ELG_DATA	Missing eligibility data
29	EL_ELGBLTY_MO_CNT	Eligible months
30	EL_PRVT_INSRNC_MO_CNT	Private insurance months
31	EL_MDCR_ANN_XOVR_OLD	Crossover code (Old Annual)
32	EL_MDCR_QTR_XOVR_OLD_1	Quarterly crossover code (Old Quarter 1)
33	EL_MDCR_QTR_XOVR_OLD_2	Quarterly crossover code (Old Quarter 2)
34	EL_MDCR_QTR_XOVR_OLD_3	Quarterly crossover code (Old Quarter 3)
35	EL_MDCR_QTR_XOVR_OLD_4	Quarterly crossover code (Old Quarter 4)
36	EL_MDCR_DUAL_ANN	Medicare dual code (Annual)
37	EL_MDCR_QTR_XOVR_99_1	Quarterly crossover code (Quarter 1)
38	EL_MDCR_QTR_XOVR_99_2	Quarterly crossover code (Quarter 2)
39	EL_MDCR_QTR_XOVR_99_3	Quarterly crossover code (Quarter 3)
40	EL_MDCR_QTR_XOVR_99_4	Quarterly crossover code (Quarter 4)
41	EL_MDCR_BEN_MO_CNT	Medicare benefic mos (from Medicare EDB)
42	MDCR_ORIG_REAS_CD	Mcare orig entitlement reason (from EDB)
43	EL_MDCR_DUAL_MO_1	Medicare dual code (Jan)
44	EL_MDCR_DUAL_MO_2	Medicare dual code (Feb)

45	EL_MDCR_DUAL_MO_3	Medicare dual code (Mar)
46	EL_MDCR_DUAL_MO_4	Medicare dual code (Apr)
47	EL_MDCR_DUAL_MO_5	Medicare dual code (May)
48	EL_MDCR_DUAL_MO_6	Medicare dual code (Jun)
49	EL_MDCR_DUAL_MO_7	Medicare dual code (Jul)
50	EL_MDCR_DUAL_MO_8	Medicare dual code (Aug)
51	EL_MDCR_DUAL_MO_9	Medicare dual code (Sep)
52	EL_MDCR_DUAL_MO_10	Medicare dual code (Oct)
53	EL_MDCR_DUAL_MO_11	Medicare dual code (Nov)
54	EL_MDCR_DUAL_MO_12	Medicare dual code (Dec)
55	SS_ELG_CD_MO_1	State specific eligibility group (Jan)
56	SS_ELG_CD_MO_2	State specific eligibility group (Feb)
57	SS_ELG_CD_MO_3	State specific eligibility group (Mar)
58	SS_ELG_CD_MO_4	State specific eligibility group (Apr)
59	SS_ELG_CD_MO_5	State specific eligibility group (May)
60	SS_ELG_CD_MO_6	State specific eligibility group (Jun)
61	SS_ELG_CD_MO_7	State specific eligibility group (Jul)
62	SS_ELG_CD_MO_8	State specific eligibility group (Aug)
63	SS_ELG_CD_MO_9	State specific eligibility group (Sep)
64	SS_ELG_CD_MO_10	State specific eligibility group (Oct)
65	SS_ELG_CD_MO_11	State specific eligibility group (Nov)
66	SS_ELG_CD_MO_12	State specific eligibility group (Dec)
67	MAX_ELG_CD_MO_1	MAX eligibility group (Jan)
68	MAX_ELG_CD_MO_2	MAX eligibility group (Feb)
69	MAX_ELG_CD_MO_3	MAX eligibility group (Mar)
70	MAX_ELG_CD_MO_4	MAX eligibility group (Apr)
71	MAX_ELG_CD_MO_5	MAX eligibility group (May)
72	MAX_ELG_CD_MO_6	MAX eligibility group (Jun)
73	MAX_ELG_CD_MO_7	MAX eligibility group (Jul)
74	MAX_ELG_CD_MO_8	MAX eligibility group (Aug)
75	MAX_ELG_CD_MO_9	MAX eligibility group (Sep)
76	MAX_ELG_CD_MO_10	MAX eligibility group (Oct)
77	MAX_ELG_CD_MO_11	MAX eligibility group (Nov)
78	MAX_ELG_CD_MO_12	MAX eligibility group (Dec)
79	EL_PVT_INS_CD_1	Private health insurance group (Jan)
80	EL_PVT_INS_CD_2	Private health insurance group (Feb)
81	EL_PVT_INS_CD_3	Private health insurance group (Mar)
82	EL_PVT_INS_CD_4	Private health insurance group (Apr)
83	EL_PVT_INS_CD_5	Private health insurance group (May)
84	EL_PVT_INS_CD_6	Private health insurance group (Jun)
85	EL_PVT_INS_CD_7	Private health insurance group (Jul)
86	EL_PVT_INS_CD_8	Private health insurance group (Aug)
87	EL_PVT_INS_CD_9	Private health insurance group (Sep)
88	EL_PVT_INS_CD_10	Private health insurance group (Oct)
89	EL_PVT_INS_CD_11	Private health insurance group (Nov)
90	EL_PVT_INS_CD_12	Private health insurance group (Dec)
91	EL_MDCR_BEN_MO_1	Medicare beneficiary (Jan)
92	EL_MDCR_BEN_MO_2	Medicare beneficiary (Feb)
93	EL_MDCR_BEN_MO_3	Medicare beneficiary (Mar)
94	EL_MDCR_BEN_MO_4	Medicare beneficiary (Apr)
95	EL_MDCR_BEN_MO_5	Medicare beneficiary (May)

96	EL_MDCR_BEN_MO_6	Medicare beneficiary (Jun)
97	EL_MDCR_BEN_MO_7	Medicare beneficiary (Jul)
98	EL_MDCR_BEN_MO_8	Medicare beneficiary (Aug)
99	EL_MDCR_BEN_MO_9	Medicare beneficiary (Sep)
100	EL_MDCR_BEN_MO_10	Medicare beneficiary (Oct)
101	EL_MDCR_BEN_MO_11	Medicare beneficiary (Nov)
102	EL_MDCR_BEN_MO_12	Medicare beneficiary (Dec)
103	EL_PPH_PLN_MO_CNT_CMCP	Prepaid plan months (comprehen plans)
104	EL_PPH_PLN_MO_CNT_DMCP	Prepaid plan months (DMCP)
105	EL_PPH_PLN_MO_CNT_BMCP	Prepaid plan months (BMCP)
106	EL_PPH_PLN_MO_CNT_PDMC	Prepaid plan months (PDMC)
107	EL_PPH_PLN_MO_CNT_LTCM	Prepaid plan months (LTCM)
108	EL_PPH_PLN_MO_CNT_AICE	Prepaid plan months (AICE)
109	EL_PPH_PLN_MO_CNT_PCCM	Prepaid plan months (PCCM)
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111	EL_PHP_ID_1_1	Prepaid plan identifier-1 (Jan)
112	EL_PHP_TYPE_2_1	Prepaid plan type-2 (Jan)
113	EL_PHP_ID_2_1	Prepaid plan identifier-2 (Jan)
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115	EL_PHP_ID_3_1	Prepaid plan identifier-3 (Jan)
116	EL_PHP_TYPE_4_1	Prepaid plan type-4 (Jan)
117	EL_PHP_ID_4_1	Prepaid plan identifier-4 (Jan)
118	EL_PHP_TYPE_1_2	Prepaid plan type-1 (Feb)
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122	EL_PHP_TYPE_3_2	Prepaid plan type-3 (Feb)
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124	EL_PHP_TYPE_4_2	Prepaid plan type-4 (Feb)
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126	EL_PHP_TYPE_1_3	Prepaid plan type-1 (Mar)
127	EL_PHP_ID_1_3	Prepaid plan identifier-1 (Mar)
128	EL_PHP_TYPE_2_3	Prepaid plan type-2 (Mar)
129	EL_PHP_ID_2_3	Prepaid plan identifier-2 (Mar)
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131	EL_PHP_ID_3_3	Prepaid plan identifier-3 (Mar)
132	EL_PHP_TYPE_4_3	Prepaid plan type-4 (Mar)
133	EL_PHP_ID_4_3	Prepaid plan identifier-4 (Mar)
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140	EL_PHP_TYPE_4_4	Prepaid plan type-4 (Apr)
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143	EL_PHP_ID_1_5	Prepaid plan identifier-1 (May)
144	EL_PHP_TYPE_2_5	Prepaid plan type-2 (May)
145	EL_PHP_ID_2_5	Prepaid plan identifier-2 (May)
146	EL_PHP_TYPE_3_5	Prepaid plan type-3 (May)

147	EL_PHP_ID_3_5	Prepaid plan identifier-3 (May)
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149	EL_PHP_ID_4_5	Prepaid plan identifier-4 (May)
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153	EL_PHP_ID_2_6	Prepaid plan identifier-2 (Jun)
154	EL_PHP_TYPE_3_6	Prepaid plan type-3 (Jun)
155	EL_PHP_ID_3_6	Prepaid plan identifier-3 (Jun)
156	EL_PHP_TYPE_4_6	Prepaid plan type-4 (Jun)
157	EL_PHP_ID_4_6	Prepaid plan identifier-4 (Jun)
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163	EL_PHP_ID_3_7	Prepaid plan identifier-3 (Jul)
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165	EL_PHP_ID_4_7	Prepaid plan identifier-4 (Jul)
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175	EL_PHP_ID_1_9	Prepaid plan identifier-1 (Sep)
176	EL_PHP_TYPE_2_9	Prepaid plan type-2 (Sep)
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179	EL_PHP_ID_3_9	Prepaid plan identifier-3 (Sep)
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183	EL_PHP_ID_1_10	Prepaid plan identifier-1 (Oct)
184	EL_PHP_TYPE_2_10	Prepaid plan type-2 (Oct)
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195	EL_PHP_ID_3_11	Prepaid plan identifier-3 (Nov)
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198	EL_PHP_TYPE_1_12	Prepaid plan type-1 (Dec)
199	EL_PHP_ID_1_12	Prepaid plan identifier-1 (Dec)
200	EL_PHP_TYPE_2_12	Prepaid plan type-2 (Dec)
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202	EL_PHP_TYPE_3_12	Prepaid plan type-3 (Dec)
203	EL_PHP_ID_3_12	Prepaid plan identifier-3 (Dec)
204	EL_PHP_TYPE_4_12	Prepaid plan type-4 (Dec)
205	EL_PHP_ID_4_12	Prepaid plan identifier-4 (Dec)
206	MC_COMBO_MO_1	Managed care combinations (Jan)
207	MC_COMBO_MO_2	Managed care combinations (Feb)
208	MC_COMBO_MO_3	Managed care combinations (Mar)
209	MC_COMBO_MO_4	Managed care combinations (Apr)
210	MC_COMBO_MO_5	Managed care combinations (May)
211	MC_COMBO_MO_6	Managed care combinations (Jun)
212	MC_COMBO_MO_7	Managed care combinations (Jul)
213	MC_COMBO_MO_8	Managed care combinations (Aug)
214	MC_COMBO_MO_9	Managed care combinations (Sep)
215	MC_COMBO_MO_10	Managed care combinations (Oct)
216	MC_COMBO_MO_11	Managed care combinations (Nov)
217	MC_COMBO_MO_12	Managed care combinations (Dec)
218	EL_DAYS_EL_CNT_1	Days of eligibility (Jan)
219	EL_DAYS_EL_CNT_2	Days of eligibility (Feb)
220	EL_DAYS_EL_CNT_3	Days of eligibility (Mar)
221	EL_DAYS_EL_CNT_4	Days of eligibility (Apr)
222	EL_DAYS_EL_CNT_5	Days of eligibility (May)
223	EL_DAYS_EL_CNT_6	Days of eligibility (Jun)
224	EL_DAYS_EL_CNT_7	Days of eligibility (Jul)
225	EL_DAYS_EL_CNT_8	Days of eligibility (Aug)
226	EL_DAYS_EL_CNT_9	Days of eligibility (Sep)
227	EL_DAYS_EL_CNT_10	Days of eligibility (Oct)
228	EL_DAYS_EL_CNT_11	Days of eligibility (Nov)
229	EL_DAYS_EL_CNT_12	Days of eligibility (Dec)
230	EL_TANF_CASH_FLG_1	TANF cash eligibility (Jan)
231	EL_TANF_CASH_FLG_2	TANF cash eligibility (Feb)
232	EL_TANF_CASH_FLG_3	TANF cash eligibility (Mar)
233	EL_TANF_CASH_FLG_4	TANF cash eligibility (Apr)
234	EL_TANF_CASH_FLG_5	TANF cash eligibility (May)
235	EL_TANF_CASH_FLG_6	TANF cash eligibility (Jun)
236	EL_TANF_CASH_FLG_7	TANF cash eligibility (Jul)
237	EL_TANF_CASH_FLG_8	TANF cash eligibility (Aug)
238	EL_TANF_CASH_FLG_9	TANF cash eligibility (Sep)
239	EL_TANF_CASH_FLG_10	TANF cash eligibility (Oct)
240	EL_TANF_CASH_FLG_11	TANF cash eligibility (Nov)
241	EL_TANF_CASH_FLG_12	TANF cash eligibility (Dec)
242	EL_RSTRCT_BNFT_FLG_1	Restricted benefits (Jan)
243	EL_RSTRCT_BNFT_FLG_2	Restricted benefits (Feb)
244	EL_RSTRCT_BNFT_FLG_3	Restricted benefits (Mar)
245	EL_RSTRCT_BNFT_FLG_4	Restricted benefits (Apr)
246	EL_RSTRCT_BNFT_FLG_5	Restricted benefits (May)
247	EL_RSTRCT_BNFT_FLG_6	Restricted benefits (Jun)
248	EL_RSTRCT_BNFT_FLG_7	Restricted benefits (Jul)

249	EL_RSTRCT_BNFT_FLG_8	Restricted benefits (Aug)
250	EL_RSTRCT_BNFT_FLG_9	Restricted benefits (Sep)
251	EL_RSTRCT_BNFT_FLG_10	Restricted benefits (Oct)
252	EL_RSTRCT_BNFT_FLG_11	Restricted benefits (Nov)
253	EL_RSTRCT_BNFT_FLG_12	Restricted benefits (Dec)
254	EL_CHIP_FLAG_1	SCHIP eligibility (Jan)
255	EL_CHIP_FLAG_2	SCHIP eligibility (Feb)
256	EL_CHIP_FLAG_3	SCHIP eligibility (Mar)
257	EL_CHIP_FLAG_4	SCHIP eligibility (Apr)
258	EL_CHIP_FLAG_5	SCHIP eligibility (May)
259	EL_CHIP_FLAG_6	SCHIP eligibility (Jun)
260	EL_CHIP_FLAG_7	SCHIP eligibility (Jul)
261	EL_CHIP_FLAG_8	SCHIP eligibility (Aug)
262	EL_CHIP_FLAG_9	SCHIP eligibility (Sep)
263	EL_CHIP_FLAG_10	SCHIP eligibility (Oct)
264	EL_CHIP_FLAG_11	SCHIP eligibility (Nov)
265	EL_CHIP_FLAG_12	SCHIP eligibility (Dec)
266	MAX_WAIVER_TYPE_1_MO_1	MAX Waiver Type Code -1 (Jan)
267	MAX_WAIVER_ID_1_MO_1	Waiver ID-1 (Jan)
268	MAX_WAIVER_TYPE_2_MO_1	MAX Waiver Type Code -2 (Jan)
269	MAX_WAIVER_ID_2_MO_1	Waiver ID-2 (Jan)
270	MAX_WAIVER_TYPE_3_MO_1	MAX Waiver Type Code -3 (Jan)
271	MAX_WAIVER_ID_3_MO_1	Waiver ID-3 (Jan)
272	MAX_WAIVER_TYPE_1_MO_2	MAX Waiver Type Code -1 (Feb)
273	MAX_WAIVER_ID_1_MO_2	Waiver ID-1 (Feb)
274	MAX_WAIVER_TYPE_2_MO_2	MAX Waiver Type Code -2 (Feb)
275	MAX_WAIVER_ID_2_MO_2	Waiver ID-2 (Feb)
276	MAX_WAIVER_TYPE_3_MO_2	MAX Waiver Type Code -3 (Feb)
277	MAX_WAIVER_ID_3_MO_2	Waiver ID-3 (Feb)
278	MAX_WAIVER_TYPE_1_MO_3	MAX Waiver Type Code -1 (Mar)
279	MAX_WAIVER_ID_1_MO_3	Waiver ID-1 (Mar)
280	MAX_WAIVER_TYPE_2_MO_3	MAX Waiver Type Code -2 (Mar)
281	MAX_WAIVER_ID_2_MO_3	Waiver ID-2 (Mar)
282	MAX_WAIVER_TYPE_3_MO_3	MAX Waiver Type Code -3 (Mar)
283	MAX_WAIVER_ID_3_MO_3	Waiver ID-3 (Mar)
284	MAX_WAIVER_TYPE_1_MO_4	MAX Waiver Type Code -1 (Apr)
285	MAX_WAIVER_ID_1_MO_4	Waiver ID-1 (Apr)
286	MAX_WAIVER_TYPE_2_MO_4	MAX Waiver Type Code -2 (Apr)
287	MAX_WAIVER_ID_2_MO_4	Waiver ID-2 (Apr)
288	MAX_WAIVER_TYPE_3_MO_4	MAX Waiver Type Code -3 (Apr)
289	MAX_WAIVER_ID_3_MO_4	Waiver ID-3 (Apr)
290	MAX_WAIVER_TYPE_1_MO_5	MAX Waiver Type Code -1 (May)
291	MAX_WAIVER_ID_1_MO_5	Waiver ID-1 (May)
292	MAX_WAIVER_TYPE_2_MO_5	MAX Waiver Type Code -2 (May)
293	MAX_WAIVER_ID_2_MO_5	Waiver ID-2 (May)
294	MAX_WAIVER_TYPE_3_MO_5	MAX Waiver Type Code -3 (May)
295	MAX_WAIVER_ID_3_MO_5	Waiver ID-3 (May)
296	MAX_WAIVER_TYPE_1_MO_6	MAX Waiver Type Code -1 (Jun)
297	MAX_WAIVER_ID_1_MO_6	Waiver ID-1 (Jun)
298	MAX_WAIVER_TYPE_2_MO_6	MAX Waiver Type Code -2 (Jun)
299	MAX_WAIVER_ID_2_MO_6	Waiver ID-2 (Jun)

300	MAX_WAIVER_TYPE_3_MO_6	MAX Waiver Type Code -3 (Jun)
301	MAX_WAIVER_ID_3_MO_6	Waiver ID-3 (Jun)
302	MAX_WAIVER_TYPE_1_MO_7	MAX Waiver Type Code -1 (Jul)
303	MAX_WAIVER_ID_1_MO_7	Waiver ID-1 (Jul)
304	MAX_WAIVER_TYPE_2_MO_7	MAX Waiver Type Code -2 (Jul)
305	MAX_WAIVER_ID_2_MO_7	Waiver ID-2 (Jul)
306	MAX_WAIVER_TYPE_3_MO_7	MAX Waiver Type Code -3 (Jul)
307	MAX_WAIVER_ID_3_MO_7	Waiver ID-3 (Jul)
308	MAX_WAIVER_TYPE_1_MO_8	MAX Waiver Type Code -1 (Aug)
309	MAX_WAIVER_ID_1_MO_8	Waiver ID-1 (Aug)
310	MAX_WAIVER_TYPE_2_MO_8	MAX Waiver Type Code -2 (Aug)
311	MAX_WAIVER_ID_2_MO_8	Waiver ID-2 (Aug)
312	MAX_WAIVER_TYPE_3_MO_8	MAX Waiver Type Code -3 (Aug)
313	MAX_WAIVER_ID_3_MO_8	Waiver ID-3 (Aug)
314	MAX_WAIVER_TYPE_1_MO_9	MAX Waiver Type Code -1 (Sep)
315	MAX_WAIVER_ID_1_MO_9	Waiver ID-1 (Sep)
316	MAX_WAIVER_TYPE_2_MO_9	MAX Waiver Type Code -2 (Sep)
317	MAX_WAIVER_ID_2_MO_9	Waiver ID-2 (Sep)
318	MAX_WAIVER_TYPE_3_MO_9	MAX Waiver Type Code -3 (Sep)
319	MAX_WAIVER_ID_3_MO_9	Waiver ID-3 (Sep)
320	MAX_WAIVER_TYPE_1_MO_10	MAX Waiver Type Code -1 (Oct)
321	MAX_WAIVER_ID_1_MO_10	Waiver ID-1 (Oct)
322	MAX_WAIVER_TYPE_2_MO_10	MAX Waiver Type Code -2 (Oct)
323	MAX_WAIVER_ID_2_MO_10	Waiver ID-2 (Oct)
324	MAX_WAIVER_TYPE_3_MO_10	MAX Waiver Type Code -3 (Oct)
325	MAX_WAIVER_ID_3_MO_10	Waiver ID-3 (Oct)
326	MAX_WAIVER_TYPE_1_MO_11	MAX Waiver Type Code -1 (Nov)
327	MAX_WAIVER_ID_1_MO_11	Waiver ID-1 (Nov)
328	MAX_WAIVER_TYPE_2_MO_11	MAX Waiver Type Code -2 (Nov)
329	MAX_WAIVER_ID_2_MO_11	Waiver ID-2 (Nov)
330	MAX_WAIVER_TYPE_3_MO_11	MAX Waiver Type Code -3 (Nov)
331	MAX_WAIVER_ID_3_MO_11	Waiver ID-3 (Nov)
332	MAX_WAIVER_TYPE_1_MO_12	MAX Waiver Type Code -1 (Dec)
333	MAX_WAIVER_ID_1_MO_12	Waiver ID-1 (Dec)
334	MAX_WAIVER_TYPE_2_MO_12	MAX Waiver Type Code -2 (Dec)
335	MAX_WAIVER_ID_2_MO_12	Waiver ID-2 (Dec)
336	MAX_WAIVER_TYPE_3_MO_12	MAX Waiver Type Code -3 (Dec)
337	MAX_WAIVER_ID_3_MO_12	Waiver ID-3 (Dec)
338	MAX_1915C_WAIVER_TYPE_LTST	Annual 1915(c) MAX Waiver Type
339	RCPNT_IND	Recipient indicator
340	TOT_IP_DSCHRG_CNT	IP discharges
341	TOT_IP_STAY_CNT	IP stays
342	TOT_IP_DAY_CNT_DSCHRG	Length of Stay (LOS) - for discharges
343	TOT_IP_DAY_CNT_STAYS	Length of Stay (LOS) - for stays
344	TOT_IP_CVR_DAY_CNT_DSCHRG	Covered days - for discharges
345	TOT_IP_CVR_DAY_CNT_STAYS	Covered days - for stays
346	TOT_LTC_CVR_DAY_CNT_AGED	Mental hospital covered days
347	TOT_LTC_CVR_DAY_CNT_PSYCH	Inpatient psych (age < 21) covered days
348	TOT_LTC_CVR_DAY_CNT_ICFMR	ICF/MR covered days
349	TOT_LTC_CVR_DAY_CNT_NF	Nursing facility covered days
350	TOT_LTC_CVR_DAY_CNT	Total LT covered days

351	TOT_MDCD_CLM_CNT	Total record count
352	TOT_MDCD_FFS_CLM_CNT	Fee-for-service claim count
353	TOT_MDCD_PREM_CLM_CNT	Premium payment claim count
354	TOT_MDCD_ENCT_CLM_CNT	Encounter record count
355	TOT_MDCD_PYMT_AMT	Total Medicaid payment amount
356	TOT_MDCD_FFS_PYMT_AMT	Fee-for-service Medicaid payment amount
357	TOT_MDCD_PREM_PYMT_AMT	Premium payment Medicaid payment amount
358	TOT_MDCD_CHRG_AMT	Charge amount
359	TOT_MDCD_TP_PYMT_AMT	Third party payment amount
360	IP_HOSP_REC_FP	Inpatient hospital records (FP)
361	IP_HOSP_PYMT_FP	Inpatient hospital payments (FP)
362	LT_REC_CNT_FP	Institutional LT care records (FP)
363	LT_PYMT_AMT_FP	Institutional LT care payments (FP)
364	OT_REC_CNT_FP	Other service records (FP)
365	OT_PYMT_AMT_FP	Other service payments (FP)
366	RX_REC_CNT_FP	Prescription drug records (FP)
367	RX_PYMT_AMT_FP	Prescription drug payments (FP)
368	TOT_REC_CNT_FP	Total records (FP)
369	TOT_PYMT_AMT_FP	Total payments (FP)
370	IP_HOSP_REC_RHC	Inpatient hospital records (RHC)
371	IP_HOSP_PYMT_RHC	Inpatient hospital payments (RHC)
372	LT_REC_CNT_RHC	Institutional LT care records (RHC)
373	LT_PYMT_AMT_RHC	Institutional LT care payments (RHC)
374	OT_REC_CNT_RHC	Other service records (RHC)
375	OT_PYMT_AMT_RHC	Other service payments (RHC)
376	RX_REC_CNT_RHC	Prescription drug records (RHC)
377	RX_PYMT_AMT_RHC	Prescription drug payments (RHC)
378	TOT_REC_CNT_RHC	Total records (RHC)
379	TOT_PYMT_AMT_RHC	Total payments (RHC)
380	IP_HOSP_REC_FQHC	Inpatient hospital records (FQHC)
381	IP_HOSP_PYMT_FQHC	Inpatient hospital payments (FQHC)
382	LT_REC_CNT_FQHC	Institutional LT care records (FQHC)
383	LT_PYMT_AMT_FQHC	Institutional LT care payments (FQHC)
384	OT_REC_CNT_FQHC	Other service records (FQHC)
385	OT_PYMT_AMT_FQHC	Other service payments (FQHC)
386	RX_REC_CNT_FQHC	Prescription drug records (FQHC)
387	RX_PYMT_AMT_FQHC	Prescription drug payments (FQHC)
388	TOT_REC_CNT_FQHC	Total records (FQHC)
389	TOT_PYMT_AMT_FQHC	Total payments (FQHC)
390	IP_HOSP_REC_IHS	Inpatient hospital records (IHS)
391	IP_HOSP_PYMT_IHS	Inpatient hospital payments (IHS)
392	LT_REC_CNT_IHS	Institutional LT care records (IHS)
393	LT_PYMT_AMT_IHS	Institutional LT care payments (IHS)
394	OT_REC_CNT_IHS	Other service records (IHS)
395	OT_PYMT_AMT_IHS	Other service payments (IHS)
396	RX_REC_CNT_IHS	Prescription drug records (IHS)
397	RX_PYMT_AMT_IHS	Prescription drug payments (IHS)
398	TOT_REC_CNT_IHS	Total records (IHS)
399	TOT_PYMT_AMT_IHS	Total payments (IHS)
400	IP_HOSP_REC_HCBCA	Inpatient hospital records (HCBCA)
401	IP_HOSP_PYMT_HCBCA	Inpatient hospital payments (HCBCA)

402	LT_REC_CNT_HCBCA	Institutional LT care records (HCBCA)
403	LT_PYMT_AMT_HCBCA	Institutional LT care payments (HCBCA)
404	OT_REC_CNT_HCBCA	Other service records (HCBCA)
405	OT_PYMT_AMT_HCBCA	Other service payments (HCBCA)
406	RX_REC_CNT_HCBCA	Prescription drug records (HCBCA)
407	RX_PYMT_AMT_HCBCA	Prescription drug payments (HCBCA)
408	TOT_REC_CNT_HCBCA	Total records (HCBCA)
409	TOT_PYMT_AMT_HCBCA	Total payments (HCBCA)
410	IP_HOSP_REC_HCBCS	Inpatient hospital records (HCBCS)
411	IP_HOSP_PYMT_HCBCS	Inpatient hospital payments (HCBCS)
412	LT_REC_CNT_HCBCS	Institutional LT care records (HCBCS)
413	LT_PYMT_AMT_HCBCS	Institutional LT care payments (HCBCS)
414	OT_REC_CNT_HCBCS	Other service records (HCBCS)
415	OT_PYMT_AMT_HCBCS	Other service payments (HCBCS)
416	RX_REC_CNT_HCBCS	Prescription drug records (HCBCS)
417	RX_PYMT_AMT_HCBCS	Prescription drug payments (HCBCS)
418	TOT_REC_CNT_HCBCS	Total records (HCBCS)
419	TOT_PYMT_AMT_HCBCS	Total payments (HCBCS)
420	RCPNT_DLVRY_CD	Delivery code
421	FEE_FOR_SRVC_IND_01	Recipient indicator (MAX TOS 01)
422	FFS_CLM_CNT_01	Claim count (MAX TOS 01)
423	FFS_PYMT_AMT_01	Medicaid payment amount (MAX TOS 01)
424	FFS_CHRG_AMT_01	Charge amount (MAX TOS 01)
425	FFS_TP_AMT_01	Third party payment amount (MAX TOS 01)
426	ENCTR_REC_CNT_01	Encounter record count (MAX TOS 01)
427	FEE_FOR_SRVC_IND_02	Recipient indicator (MAX TOS 02)
428	FFS_CLM_CNT_02	Claim count (MAX TOS 02)
429	FFS_PYMT_AMT_02	Medicaid payment amount (MAX TOS 02)
430	FFS_CHRG_AMT_02	Charge amount (MAX TOS 02)
431	FFS_TP_AMT_02	Third party payment amount (MAX TOS 02)
432	ENCTR_REC_CNT_02	Encounter record count (MAX TOS 02)
433	FEE_FOR_SRVC_IND_04	Recipient indicator (MAX TOS 04)
434	FFS_CLM_CNT_04	Claim count (MAX TOS 04)
435	FFS_PYMT_AMT_04	Medicaid payment amount (MAX TOS 04)
436	FFS_CHRG_AMT_04	Charge amount (MAX TOS 04)
437	FFS_TP_AMT_04	Third party payment amount (MAX TOS 04)
438	ENCTR_REC_CNT_04	Encounter record count (MAX TOS 04)
439	FEE_FOR_SRVC_IND_05	Recipient indicator (MAX TOS 05)
440	FFS_CLM_CNT_05	Claim count (MAX TOS 05)
441	FFS_PYMT_AMT_05	Medicaid payment amount (MAX TOS 05)
442	FFS_CHRG_AMT_05	Charge amount (MAX TOS 05)
443	FFS_TP_AMT_05	Third party payment amount (MAX TOS 05)
444	ENCTR_REC_CNT_05	Encounter record count (MAX TOS 05)
445	FEE_FOR_SRVC_IND_07	Recipient indicator (MAX TOS 07)
446	FFS_CLM_CNT_07	Claim count (MAX TOS 07)
447	FFS_PYMT_AMT_07	Medicaid payment amount (MAX TOS 07)
448	FFS_CHRG_AMT_07	Charge amount (MAX TOS 07)
449	FFS_TP_AMT_07	Third party payment amount (MAX TOS 07)
450	ENCTR_REC_CNT_07	Encounter record count (MAX TOS 07)
451	FEE_FOR_SRVC_IND_08	Recipient indicator (MAX TOS 08)
452	FFS_CLM_CNT_08	Claim count (MAX TOS 08)

453	FFS_PYMT_AMT_08	Medicaid payment amount (MAX TOS 08)
454	FFS_CHRG_AMT_08	Charge amount (MAX TOS 08)
455	FFS_TP_AMT_08	Third party payment amount (MAX TOS 08)
456	ENCTR_REC_CNT_08	Encounter record count (MAX TOS 08)
457	FEE_FOR_SRVC_IND_09	Recipient indicator (MAX TOS 09)
458	FFS_CLM_CNT_09	Claim count (MAX TOS 09)
459	FFS_PYMT_AMT_09	Medicaid payment amount (MAX TOS 09)
460	FFS_CHRG_AMT_09	Charge amount (MAX TOS 09)
461	FFS_TP_AMT_09	Third party payment amount (MAX TOS 09)
462	ENCTR_REC_CNT_09	Encounter record count (MAX TOS 09)
463	FEE_FOR_SRVC_IND_10	Recipient indicator (MAX TOS 10)
464	FFS_CLM_CNT_10	Claim count (MAX TOS 10)
465	FFS_PYMT_AMT_10	Medicaid payment amount (MAX TOS 10)
466	FFS_CHRG_AMT_10	Charge amount (MAX TOS 10)
467	FFS_TP_AMT_10	Third party payment amount (MAX TOS 10)
468	ENCTR_REC_CNT_10	Encounter record count (MAX TOS 10)
469	FEE_FOR_SRVC_IND_11	Recipient indicator (MAX TOS 11)
470	FFS_CLM_CNT_11	Claim count (MAX TOS 11)
471	FFS_PYMT_AMT_11	Medicaid payment amount (MAX TOS 11)
472	FFS_CHRG_AMT_11	Charge amount (MAX TOS 11)
473	FFS_TP_AMT_11	Third party payment amount (MAX TOS 11)
474	ENCTR_REC_CNT_11	Encounter record count (MAX TOS 11)
475	FEE_FOR_SRVC_IND_12	Recipient indicator (MAX TOS 12)
476	FFS_CLM_CNT_12	Claim count (MAX TOS 12)
477	FFS_PYMT_AMT_12	Medicaid payment amount (MAX TOS 12)
478	FFS_CHRG_AMT_12	Charge amount (MAX TOS 12)
479	FFS_TP_AMT_12	Third party payment amount (MAX TOS 12)
480	ENCTR_REC_CNT_12	Encounter record count (MAX TOS 12)
481	FEE_FOR_SRVC_IND_13	Recipient indicator (MAX TOS 13)
482	FFS_CLM_CNT_13	Claim count (MAX TOS 13)
483	FFS_PYMT_AMT_13	Medicaid payment amount (MAX TOS 13)
484	FFS_CHRG_AMT_13	Charge amount (MAX TOS 13)
485	FFS_TP_AMT_13	Third party payment amount (MAX TOS 13)
486	ENCTR_REC_CNT_13	Encounter record count (MAX TOS 13)
487	FEE_FOR_SRVC_IND_15	Recipient indicator (MAX TOS 15)
488	FFS_CLM_CNT_15	Claim count (MAX TOS 15)
489	FFS_PYMT_AMT_15	Medicaid payment amount (MAX TOS 15)
490	FFS_CHRG_AMT_15	Charge amount (MAX TOS 15)
491	FFS_TP_AMT_15	Third party payment amount (MAX TOS 15)
492	ENCTR_REC_CNT_15	Encounter record count (MAX TOS 15)
493	FEE_FOR_SRVC_IND_16	Recipient indicator (MAX TOS 16)
494	FFS_CLM_CNT_16	Claim count (MAX TOS 16)
495	FFS_PYMT_AMT_16	Medicaid payment amount (MAX TOS 16)
496	FFS_CHRG_AMT_16	Charge amount (MAX TOS 16)
497	FFS_TP_AMT_16	Third party payment amount (MAX TOS 16)
498	ENCTR_REC_CNT_16	Encounter record count (MAX TOS 16)
499	FEE_FOR_SRVC_IND_19	Recipient indicator (MAX TOS 19)
500	FFS_CLM_CNT_19	Claim count (MAX TOS 19)
501	FFS_PYMT_AMT_19	Medicaid payment amount (MAX TOS 19)
502	FFS_CHRG_AMT_19	Charge amount (MAX TOS 19)
503	FFS_TP_AMT_19	Third party payment amount (MAX TOS 19)

504	ENCTR_REC_CNT_19	Encounter record count (MAX TOS 19)
505	FEE_FOR_SRVC_IND_24	Recipient indicator (MAX TOS 24)
506	FFS_CLM_CNT_24	Claim count (MAX TOS 24)
507	FFS_PYMT_AMT_24	Medicaid payment amount (MAX TOS 24)
508	FFS_CHRG_AMT_24	Charge amount (MAX TOS 24)
509	FFS_TP_AMT_24	Third party payment amount (MAX TOS 24)
510	ENCTR_REC_CNT_24	Encounter record count (MAX TOS 24)
511	FEE_FOR_SRVC_IND_25	Recipient indicator (MAX TOS 25)
512	FFS_CLM_CNT_25	Claim count (MAX TOS 25)
513	FFS_PYMT_AMT_25	Medicaid payment amount (MAX TOS 25)
514	FFS_CHRG_AMT_25	Charge amount (MAX TOS 25)
515	FFS_TP_AMT_25	Third party payment amount (MAX TOS 25)
516	ENCTR_REC_CNT_25	Encounter record count (MAX TOS 25)
517	FEE_FOR_SRVC_IND_26	Recipient indicator (MAX TOS 26)
518	FFS_CLM_CNT_26	Claim count (MAX TOS 26)
519	FFS_PYMT_AMT_26	Medicaid payment amount (MAX TOS 26)
520	FFS_CHRG_AMT_26	Charge amount (MAX TOS 26)
521	FFS_TP_AMT_26	Third party payment amount (MAX TOS 26)
522	ENCTR_REC_CNT_26	Encounter record count (MAX TOS 26)
523	FEE_FOR_SRVC_IND_30	Recipient indicator (MAX TOS 30)
524	FFS_CLM_CNT_30	Claim count (MAX TOS 30)
525	FFS_PYMT_AMT_30	Medicaid payment amount (MAX TOS 30)
526	FFS_CHRG_AMT_30	Charge amount (MAX TOS 30)
527	FFS_TP_AMT_30	Third party payment amount (MAX TOS 30)
528	ENCTR_REC_CNT_30	Encounter record count (MAX TOS 30)
529	FEE_FOR_SRVC_IND_31	Recipient indicator (MAX TOS 31)
530	FFS_CLM_CNT_31	Claim count (MAX TOS 31)
531	FFS_PYMT_AMT_31	Medicaid payment amount (MAX TOS 31)
532	FFS_CHRG_AMT_31	Charge amount (MAX TOS 31)
533	FFS_TP_AMT_31	Third party payment amount (MAX TOS 31)
534	ENCTR_REC_CNT_31	Encounter record count (MAX TOS 31)
535	FEE_FOR_SRVC_IND_33	Recipient indicator (MAX TOS 33)
536	FFS_CLM_CNT_33	Claim count (MAX TOS 33)
537	FFS_PYMT_AMT_33	Medicaid payment amount (MAX TOS 33)
538	FFS_CHRG_AMT_33	Charge amount (MAX TOS 33)
539	FFS_TP_AMT_33	Third party payment amount (MAX TOS 33)
540	ENCTR_REC_CNT_33	Encounter record count (MAX TOS 33)
541	FEE_FOR_SRVC_IND_34	Recipient indicator (MAX TOS 34)
542	FFS_CLM_CNT_34	Claim count (MAX TOS 34)
543	FFS_PYMT_AMT_34	Medicaid payment amount (MAX TOS 34)
544	FFS_CHRG_AMT_34	Charge amount (MAX TOS 34)
545	FFS_TP_AMT_34	Third party payment amount (MAX TOS 34)
546	ENCTR_REC_CNT_34	Encounter record count (MAX TOS 34)
547	FEE_FOR_SRVC_IND_35	Recipient indicator (MAX TOS 35)
548	FFS_CLM_CNT_35	Claim count (MAX TOS 35)
549	FFS_PYMT_AMT_35	Medicaid payment amount (MAX TOS 35)
550	FFS_CHRG_AMT_35	Charge amount (MAX TOS 35)
551	FFS_TP_AMT_35	Third party payment amount (MAX TOS 35)
552	ENCTR_REC_CNT_35	Encounter record count (MAX TOS 35)
553	FEE_FOR_SRVC_IND_36	Recipient indicator (MAX TOS 36)
554	FFS_CLM_CNT_36	Claim count (MAX TOS 36)

555	FFS_PYMT_AMT_36	Medicaid payment amount (MAX TOS 36)
556	FFS_CHRG_AMT_36	Charge amount (MAX TOS 36)
557	FFS_TP_AMT_36	Third party payment amount (MAX TOS 36)
558	ENCTR_REC_CNT_36	Encounter record count (MAX TOS 36)
559	FEE_FOR_SRVC_IND_37	Recipient indicator (MAX TOS 37)
560	FFS_CLM_CNT_37	Claim count (MAX TOS 37)
561	FFS_PYMT_AMT_37	Medicaid payment amount (MAX TOS 37)
562	FFS_CHRG_AMT_37	Charge amount (MAX TOS 37)
563	FFS_TP_AMT_37	Third party payment amount (MAX TOS 37)
564	ENCTR_REC_CNT_37	Encounter record count (MAX TOS 37)
565	FEE_FOR_SRVC_IND_38	Recipient indicator (MAX TOS 38)
566	FFS_CLM_CNT_38	Claim count (MAX TOS 38)
567	FFS_PYMT_AMT_38	Medicaid payment amount (MAX TOS 38)
568	FFS_CHRG_AMT_38	Charge amount (MAX TOS 38)
569	FFS_TP_AMT_38	Third party payment amount (MAX TOS 38)
570	ENCTR_REC_CNT_38	Encounter record count (MAX TOS 38)
571	FEE_FOR_SRVC_IND_39	Recipient indicator (MAX TOS 39)
572	FFS_CLM_CNT_39	Claim count (MAX TOS 39)
573	FFS_PYMT_AMT_39	Medicaid payment amount (MAX TOS 39)
574	FFS_CHRG_AMT_39	Charge amount (MAX TOS 39)
575	FFS_TP_AMT_39	Third party payment amount (MAX TOS 39)
576	ENCTR_REC_CNT_39	Encounter record count (MAX TOS 39)
577	FEE_FOR_SRVC_IND_51	Recipient indicator (MAX TOS 51)
578	FFS_CLM_CNT_51	Claim count (MAX TOS 51)
579	FFS_PYMT_AMT_51	Medicaid payment amount (MAX TOS 51)
580	FFS_CHRG_AMT_51	Charge amount (MAX TOS 51)
581	FFS_TP_AMT_51	Third party payment amount (MAX TOS 51)
582	ENCTR_REC_CNT_51	Encounter record count (MAX TOS 51)
583	FEE_FOR_SRVC_IND_52	Recipient indicator (MAX TOS 52)
584	FFS_CLM_CNT_52	Claim count (MAX TOS 52)
585	FFS_PYMT_AMT_52	Medicaid payment amount (MAX TOS 52)
586	FFS_CHRG_AMT_52	Charge amount (MAX TOS 52)
587	FFS_TP_AMT_52	Third party payment amount (MAX TOS 52)
588	ENCTR_REC_CNT_52	Encounter record count (MAX TOS 52)
589	FEE_FOR_SRVC_IND_53	Recipient indicator (MAX TOS 53)
590	FFS_CLM_CNT_53	Claim count (MAX TOS 53)
591	FFS_PYMT_AMT_53	Medicaid payment amount (MAX TOS 53)
592	FFS_CHRG_AMT_53	Charge amount (MAX TOS 53)
593	FFS_TP_AMT_53	Third party payment amount (MAX TOS 53)
594	ENCTR_REC_CNT_53	Encounter record count (MAX TOS 53)
595	FEE_FOR_SRVC_IND_54	Recipient indicator (MAX TOS 54)
596	FFS_CLM_CNT_54	Claim count (MAX TOS 54)
597	FFS_PYMT_AMT_54	Medicaid payment amount (MAX TOS 54)
598	FFS_CHRG_AMT_54	Charge amount (MAX TOS 54)
599	FFS_TP_AMT_54	Third party payment amount (MAX TOS 54)
600	ENCTR_REC_CNT_54	Encounter record count (MAX TOS 54)
601	FEE_FOR_SRVC_IND_99	Recipient indicator (Unknown)
602	FFS_CLM_CNT_99	Claim count (Unknown)
603	FFS_PYMT_AMT_99	Medicaid payment amount (Unknown)
604	FFS_CHRG_AMT_99	Charge amount (Unknown)
605	FFS_TP_AMT_99	Third party payment amount (Unknown)

606	ENCTR_REC_CNT_99	Encounter record count (Unknown)
607	CLTC_FFS_PYMT_AMT_11	Medicaid payment amount (CLTC 11)
608	CLTC_FFS_PYMT_AMT_12	Medicaid payment amount (CLTC 12)
609	CLTC_FFS_PYMT_AMT_13	Medicaid payment amount (CLTC 13)
610	CLTC_FFS_PYMT_AMT_14	Medicaid payment amount (CLTC 14)
611	CLTC_FFS_PYMT_AMT_15	Medicaid payment amount (CLTC 15)
612	CLTC_FFS_PYMT_AMT_16	Medicaid payment amount (CLTC 16)
613	CLTC_FFS_PYMT_AMT_17	Medicaid payment amount (CLTC 17)
614	CLTC_FFS_PYMT_AMT_18	Medicaid payment amount (CLTC 18)
615	CLTC_FFS_PYMT_AMT_19	Medicaid payment amount (CLTC 19)
616	CLTC_FFS_PYMT_AMT_20	Medicaid payment amount (CLTC 20)
617	CLTC_FFS_PYMT_AMT_30	Medicaid payment amount (CLTC 30)
618	CLTC_FFS_PYMT_AMT_31	Medicaid payment amount (CLTC 31)
619	CLTC_FFS_PYMT_AMT_32	Medicaid payment amount (CLTC 32)
620	CLTC_FFS_PYMT_AMT_33	Medicaid payment amount (CLTC 33)
621	CLTC_FFS_PYMT_AMT_34	Medicaid payment amount (CLTC 34)
622	CLTC_FFS_PYMT_AMT_35	Medicaid payment amount (CLTC 35)
623	CLTC_FFS_PYMT_AMT_36	Medicaid payment amount (CLTC 36)
624	CLTC_FFS_PYMT_AMT_37	Medicaid payment amount (CLTC 37)
625	CLTC_FFS_PYMT_AMT_38	Medicaid payment amount (CLTC 38)
626	CLTC_FFS_PYMT_AMT_39	Medicaid payment amount (CLTC 39)
627	CLTC_FFS_PYMT_AMT_40	Medicaid payment amount (CLTC 40)
628	PREM_PYMT_IND_HMO	Premium payment indicator (HMO/HIO)
629	PREM_PYMT_REC_CNT_HMO	Premium payment records (HMO/HIO)
630	PREM_MDCD_PYMT_AMT_HMO	Medicaid premium payments (HMO/HIO)
631	PREM_PYMT_IND_PHP	Premium payment indicator (PHP)
632	PREM_PYMT_REC_CNT_PHP	Premium payment records (PHP)
633	PREM_MDCD_PYMT_AMT_PHP	Medicaid premium payments (PHP)
634	PREM_PYMT_IND_PCCM	Premium payment indicator (PCCM)
635	PREM_PYMT_REC_CNT_PCCM	Premium payment records (PCCM)
636	PREM_MDCD_PYMT_AMT_PCCM	Medicaid premium payments (PCCM)
637	SSA_DOD	Date of death (from SSA Death Master File)
638	EL_MDCR_ANN_XOVR_99	Crossover code (Annual)
639	EL_MDCR_XOVR_MO_1	Medicare crossover code (Jan)
640	EL_MDCR_XOVR_MO_2	Medicare crossover code (Feb)
641	EL_MDCR_XOVR_MO_3	Medicare crossover code (Mar)
642	EL_MDCR_XOVR_MO_4	Medicare crossover code (Apr)
643	EL_MDCR_XOVR_MO_5	Medicare crossover code (May)
644	EL_MDCR_XOVR_MO_6	Medicare crossover code (Jun)
645	EL_MDCR_XOVR_MO_7	Medicare crossover code (Jul)
646	EL_MDCR_XOVR_MO_8	Medicare crossover code (Aug)
647	EL_MDCR_XOVR_MO_9	Medicare crossover code (Sep)
648	EL_MDCR_XOVR_MO_10	Medicare crossover code (Oct)
649	EL_MDCR_XOVR_MO_11	Medicare crossover code (Nov)
650	EL_MDCR_XOVR_MO_12	Medicare crossover code (Dec)
651	HCBS_TXNMY_PYMT_AMT_01	Home and Community-Based Services (HCBS)
652	HCBS_TXNMY_PYMT_AMT_02	Home and Community-Based Services (HCBS)
653	HCBS_TXNMY_PYMT_AMT_03	Home and Community-Based Services (HCBS)
654	HCBS_TXNMY_PYMT_AMT_04	Home and Community-Based Services (HCBS)
655	HCBS_TXNMY_PYMT_AMT_05	Home and Community-Based Services (HCBS)
656	HCBS_TXNMY_PYMT_AMT_06	Home and Community-Based Services (HCBS)

657	HCBS_TXNMY_PYMT_AMT_07	Home and Community-Based Services (HCBS)
658	HCBS_TXNMY_PYMT_AMT_08	Home and Community-Based Services (HCBS)
659	HCBS_TXNMY_PYMT_AMT_09	Home and Community-Based Services (HCBS)
660	HCBS_TXNMY_PYMT_AMT_10	Home and Community-Based Services (HCBS)
661	HCBS_TXNMY_PYMT_AMT_11	Home and Community-Based Services (HCBS)
662	HCBS_TXNMY_PYMT_AMT_12	Home and Community-Based Services (HCBS)
663	HCBS_TXNMY_PYMT_AMT_13	Home and Community-Based Services (HCBS)
664	HCBS_TXNMY_PYMT_AMT_14	Home and Community-Based Services (HCBS)
665	HCBS_TXNMY_PYMT_AMT_15	Home and Community-Based Services (HCBS)
666	HCBS_TXNMY_PYMT_AMT_16	Home and Community-Based Services (HCBS)
667	HCBS_TXNMY_PYMT_AMT_17	Home and Community-Based Services (HCBS)
668	HCBS_TXNMY_PYMT_AMT_18	Home and Community-Based Services (HCBS)

Medicaid Analytic Extract (MAX) Prescription Drug File Variables

Column	Variable Name	Label
1	BENE_ID	Encrypted 723 CCW Beneficiary ID
2	MSIS_ID	Encrypted MSIS Identification Number
3	STATE_CD	State
4	YR_NUM	Year of MAX Record
5	EL_DOB	Birth date
6	EL_SEX_CD	Sex
7	EL_RACE_ETHNCY_CD	Race/ethnicity (from MSIS)
8	RACE_CODE_1	Race - White (from MSIS)
9	RACE_CODE_2	Race - Black (from MSIS)
10	RACE_CODE_3	Race - Am Indian/Alaskan (from MSIS)
11	RACE_CODE_4	Race - Asian (from MSIS)
12	RACE_CODE_5	Race - Hawaiian/Pac) Islands (from MSIS)
13	ETHNICITY_CODE	Ethnicity - Hispanic (from MSIS)
14	EL_SS_ELGBLTY_CD_LTST	State specific eligibility - most recent
15	EL_SS_ELGBLTY_CD_MO	State specific eligibility - mo of svc
16	EL_MAX_ELGBLTY_CD_LTST	MAX eligibility - most recent
17	EL_MAX_ELGBLTY_CD_MO	MAX eligibility - mo of svc
18	EL_MDCR_ANN_XOVR_OLD	Crossover code (Annual) old values
19	EL_MDCR_XOVR_CLM_BSD_CD	Crossover code (from claims only)
20	MSNG_ELG_DATA	Missing eligibility data
21	EL_MDCR_ANN_XOVR_99	Crossover code (Annual)
22	MSIS_TOS	MSIS Type of Service (TOS)
23	MSIS_TOP	MSIS Type of Program (TOP)
24	MAX_TOS	MAX Type of Service (TOS)
25	PRVDR_ID_NMBR	Billing provider identification number
26	NPI	National Provider Identifier
27	TAXONOMY	Provider Taxonomy
28	TYPE_CLM_CD	Type of claim
29	ADJUST_CD	Adjustment code
30	PHP_TYPE	Managed care type of plan code
31	PHP_ID	Managed care plan identification code
32	MDCD_PYMT_AMT	Medicaid payment amount
33	TP_PYMT_AMT	Third party payment amount
34	PYMT_DT	Payment/adjudication date
35	CHRG_AMT	Charge amount
36	PHP_VAL	Prepaid plan value
37	MDCR_COINSUR_PYMT_AMT	Medicare coinsurance payment amount
38	MDCR_DED_PYMT_AMT	Medicare deductible payment amount
39	PRES_PHYSICIAN_ID_NUM	Prescribing physician id number
40	PRSC_WRTE_DT	Prescribed date
41	PRSCRPTN_FILL_DT	Prescription fill date
42	NEW_REFILL_IND	New or refill indicator
43	NDC	National Drug Code (NDC)
44	QTY_SRVC_UNITS	Quantity of service
45	DAYS_SUPPLY	Days supply
46	NDC_FORMT_IND	NDC Format
47	DRUG_CLASS_CD	Drug Class

48	MULTI_SRCE_CD	Multi Source Code
49	HICL_THRTPC_CTGRY	HICL
50	THRTPC_CLASS_CD_SPCFC	Therapeutic Class-Specific
51	THRTPC_CLASS_CD_GENERIC	Therapeutic Class-Generic
52	AMER_HSPTL_FRMLRY_SYS_CD	American Hospital Formulary code
53	SMART_KEY	Smart Key
54	MEDISPAN_DRG_CTGRY	Medispan code
55	OVER_COUNTER_IND	Over-the-counter indicator
56	GCN_SEQNO	Clinical Formulation ID
57	HICL_SEQNO	Ingredient List ID
58	HIC3	HTCC Code
59	HIC3_SEQN	HTCC Sequence Number

Medicaid Analytic Extract (MAX) Inpatient File Variables

Column	Variable Name	Label
1	BENE_ID	Encrypted 723 CCW Beneficiary ID
2	MSIS_ID	Encrypted MSIS Identification Number
3	STATE_CD	State
4	YR_NUM	Year of MAX Record
5	EL_DOB	Birth date
6	EL_SEX_CD	Sex
7	EL_RACE_ETHNCY_CD	Race/ethnicity (from MSIS)
8	RACE_CODE_1	Race - White (from MSIS)
9	RACE_CODE_2	Race - Black (from MSIS)
10	RACE_CODE_3	Race - Am Indian/Alaskan (from MSIS)
11	RACE_CODE_4	Race - Asian (from MSIS)
12	RACE_CODE_5	Race - Hawaiian/Pac) Islands (from MSIS)
13	ETHNICITY_CODE	Ethnicity - Hispanic (from MSIS)
14	EL_SS_ELGBLTY_CD_LTST	State specific eligibility - most recent
15	EL_SS_ELGBLTY_CD_MO	State specific eligibility - mo of svc
16	EL_MAX_ELGBLTY_CD_LTST	MAX eligibility - most recent
17	EL_MAX_ELGBLTY_CD_MO	MAX eligibility - mo of svc
18	EL_MDCR_ANN_XOVR_OLD	Crossover code (Annual) old values
19	MSNG_ELG_DATA	Missing eligibility data
20	EL_MDCR_XOVR_CLM_BSD_CD	Crossover code (from claims only)
21	EL_MDCR_ANN_XOVR_99	Crossover code (Annual)
22	MSIS_TOS	MSIS Type of Service (TOS)
23	MSIS_TOP	MSIS Type of Program (TOP)
24	MAX_TOS	MAX Type of Service (TOS)
25	PRVDR_ID_NMBR	Billing provider identification number
26	NPI	National Provider Identifier
27	TAXONOMY	Provider Taxonomy
28	TYPE_CLM_CD	Type of claim
29	ADJUST_CD	Adjustment code
30	PHP_TYPE	Managed care type of plan code
31	PHP_ID	Managed care plan identification code
32	MDCD_PYMT_AMT	Medicaid payment amount
33	TP_PYMT_AMT	Third party payment amount
34	PYMT_DT	Payment/adjudication date
35	CHRG_AMT	Charge amount
36	PHP_VAL	Prepaid plan value
37	MDCR_COINSUR_PYMT_AMT	Medicare coinsurance payment amount
38	MDCR_DED_PYMT_AMT	Medicare deductible payment amount
39	ADMSN_DT	Admission date
40	SRVC_BGN_DT	Beginning date of service
41	SRVC_END_DT	Ending date of service
42	DIAG_CD_1	Principle Diagnosis code
43	DIAG_CD_2	Diagnosis codes (2nd diagnosis)
44	DIAG_CD_3	Diagnosis codes (3rd diagnosis)
45	DIAG_CD_4	Diagnosis codes (4th diagnosis)

46	DIAG_CD_5	Diagnosis codes (5th diagnosis)
47	DIAG_CD_6	Diagnosis codes (6th diagnosis)
48	DIAG_CD_7	Diagnosis codes (7th diagnosis)
49	DIAG_CD_8	Diagnosis codes (8th diagnosis)
50	DIAG_CD_9	Diagnosis codes (9th diagnosis)
51	PRNCPL_PRCDR_DT	Principle procedure date
52	PRCDR_CD_SYS_1	Procedure code system- principal
53	PRCDR_CD_1	Principle procedure code
54	PRCDR_CD_SYS_2	Procedure code system (2nd procedure)
55	PRCDR_CD_2	Procedure code (2nd procedure)
56	PRCDR_CD_SYS_3	Procedure code system (3rd procedure)
57	PRCDR_CD_3	Procedure code (3rd procedure)
58	PRCDR_CD_SYS_4	Procedure code system (4th procedure)
59	PRCDR_CD_4	Procedure code (4th procedure)
60	PRCDR_CD_SYS_5	Procedure code system (5th procedure)
61	PRCDR_CD_5	Procedure code (5th procedure)
62	PRCDR_CD_SYS_6	Procedure code system (6th procedure)
63	PRCDR_CD_6	Procedure code (6th procedure)
64	RCPNT_DLVRY_CD	Delivery code
65	MDCD_CVRD_IP_DAYS	Medicaid covered inpatient days
66	PATIENT_STATUS_CD	Patient status
67	DRG_REL_GROUP_IND	Diagnosis Related Group (DRG) indicator
68	DRG_REL_GROUP	Diagnosis Related Group (DRG)
69	UB_92_REV_CD_GP_1	UB-92 revenue code (1st)
70	UB_92_REV_CD_CHGS_1	UB-92 revenue code charge (1st)
71	UB_92_REV_CD_UNITS_1	UB-92 revenue code units (1st)
72	UB_92_REV_CD_GP_2	UB-92 revenue code (2nd)
73	UB_92_REV_CD_CHGS_2	UB-92 revenue code charge (2nd)
74	UB_92_REV_CD_UNITS_2	UB-92 revenue code units (2nd)
75	UB_92_REV_CD_GP_3	UB-92 revenue code (3rd)
76	UB_92_REV_CD_CHGS_3	UB-92 revenue code charge (3rd)
77	UB_92_REV_CD_UNITS_3	UB-92 revenue code units (3rd)
78	UB_92_REV_CD_GP_4	UB-92 revenue code (4th)
79	UB_92_REV_CD_CHGS_4	UB-92 revenue code charge (4th)
80	UB_92_REV_CD_UNITS_4	UB-92 revenue code units (4th)
81	UB_92_REV_CD_GP_5	UB-92 revenue code (5th)
82	UB_92_REV_CD_CHGS_5	UB-92 revenue code charge (5th)
83	UB_92_REV_CD_UNITS_5	UB-92 revenue code units (5th)
84	UB_92_REV_CD_GP_6	UB-92 revenue code (6th)
85	UB_92_REV_CD_CHGS_6	UB-92 revenue code charge (6th)
86	UB_92_REV_CD_UNITS_6	UB-92 revenue code units (6th)
87	UB_92_REV_CD_GP_7	UB-92 revenue code (7th)
88	UB_92_REV_CD_CHGS_7	UB-92 revenue code charge (7th)
89	UB_92_REV_CD_UNITS_7	UB-92 revenue code units (7th)
90	UB_92_REV_CD_GP_8	UB-92 revenue code (8th)
91	UB_92_REV_CD_CHGS_8	UB-92 revenue code charge (8th)
92	UB_92_REV_CD_UNITS_8	UB-92 revenue code units (8th)
93	UB_92_REV_CD_GP_9	UB-92 revenue code (9th)
94	UB_92_REV_CD_CHGS_9	UB-92 revenue code charge (9th)
95	UB_92_REV_CD_UNITS_9	UB-92 revenue code units (9th)
96	UB_92_REV_CD_GP_10	UB-92 revenue code (10th)

97	UB_92_REV_CD_CHGS_10	UB-92 revenue code charge (10th)
98	UB_92_REV_CD_UNITS_10	UB-92 revenue code units (10th)
99	UB_92_REV_CD_GP_11	UB-92 revenue code (11th)
100	UB_92_REV_CD_CHGS_11	UB-92 revenue code charge (11th)
101	UB_92_REV_CD_UNITS_11	UB-92 revenue code units (11th)
102	UB_92_REV_CD_GP_12	UB-92 revenue code (12th)
103	UB_92_REV_CD_CHGS_12	UB-92 revenue code charge (12th)
104	UB_92_REV_CD_UNITS_12	UB-92 revenue code units (12th)
105	UB_92_REV_CD_GP_13	UB-92 revenue code (13th)
106	UB_92_REV_CD_CHGS_13	UB-92 revenue code charge (13th)
107	UB_92_REV_CD_UNITS_13	UB-92 revenue code units (13th)
108	UB_92_REV_CD_GP_14	UB-92 revenue code (14th)
109	UB_92_REV_CD_CHGS_14	UB-92 revenue code charge (14th)
110	UB_92_REV_CD_UNITS_14	UB-92 revenue code units (14th)
111	UB_92_REV_CD_GP_15	UB-92 revenue code (15th)
112	UB_92_REV_CD_CHGS_15	UB-92 revenue code charge (15th)
113	UB_92_REV_CD_UNITS_15	UB-92 revenue code units (15th)
114	UB_92_REV_CD_GP_16	UB-92 revenue code (16th)
115	UB_92_REV_CD_CHGS_16	UB-92 revenue code charge (16th)
116	UB_92_REV_CD_UNITS_16	UB-92 revenue code units (16th)
117	UB_92_REV_CD_GP_17	UB-92 revenue code (17th)
118	UB_92_REV_CD_CHGS_17	UB-92 revenue code charge (17th)
119	UB_92_REV_CD_UNITS_17	UB-92 revenue code units (17th)
120	UB_92_REV_CD_GP_18	UB-92 revenue code (18th)
121	UB_92_REV_CD_CHGS_18	UB-92 revenue code charge (18th)
122	UB_92_REV_CD_UNITS_18	UB-92 revenue code units (18th)
123	UB_92_REV_CD_GP_19	UB-92 revenue code (19th)
124	UB_92_REV_CD_CHGS_19	UB-92 revenue code charge (19th)
125	UB_92_REV_CD_UNITS_19	UB-92 revenue code units (19th)
126	UB_92_REV_CD_GP_20	UB-92 revenue code (20th)
127	UB_92_REV_CD_CHGS_20	UB-92 revenue code charge (20th)
128	UB_92_REV_CD_UNITS_20	UB-92 revenue code units (20th)
129	UB_92_REV_CD_GP_21	UB-92 revenue code (21st)
130	UB_92_REV_CD_CHGS_21	UB-92 revenue code charge (21st)
131	UB_92_REV_CD_UNITS_21	UB-92 revenue code units (21st)
132	UB_92_REV_CD_GP_22	UB-92 revenue code (22nd)
133	UB_92_REV_CD_CHGS_22	UB-92 revenue code charge (22nd)
134	UB_92_REV_CD_UNITS_22	UB-92 revenue code units (22nd)
135	UB_92_REV_CD_GP_23	UB-92 revenue code (23rd)
136	UB_92_REV_CD_CHGS_23	UB-92 revenue code charge (23rd)
137	UB_92_REV_CD_UNITS_23	UB-92 revenue code units (23rd)

Medicaid Analytic Extract (MAX) Long Term Care File Variables

Column	Variable Name	Label
1	BENE_ID	Encrypted 723 CCW Beneficiary ID
2	MSIS_ID	Encrypted MSIS Identification Number
3	STATE_CD	State
4	YR_NUM	Year of MAX Record
5	EL_DOB	Birth date
6	EL_SEX_CD	Sex
7	EL_RACE_ETHNCY_CD	Race/ethnicity (from MSIS)
8	RACE_CODE_1	Race - White (from MSIS)
9	RACE_CODE_2	Race - Black (from MSIS)
10	RACE_CODE_3	Race - Am Indian/Alaskan (from MSIS)
11	RACE_CODE_4	Race - Asian (from MSIS)
12	RACE_CODE_5	Race - Hawaiian/Pac) Islands (from MSIS)
13	ETHNICITY_CODE	Ethnicity - Hispanic (from MSIS)
14	EL_SS_ELGBLTY_CD_LTST	State specific eligibility - most recent
15	EL_SS_ELGBLTY_CD_MO	State specific eligibility - mo of svc
16	EL_MAX_ELGBLTY_CD_LTST	MAX eligibility - most recent
17	EL_MAX_ELGBLTY_CD_MO	MAX eligibility - mo of svc
18	EL_MDCR_ANN_XOVR_OLD	Crossover code (Annual) old values
19	MSNG_ELG_DATA	Missing eligibility data
20	EL_MDCR_XOVR_CLM_BSD_CD	Crossover code (from claims only)
21	EL_MDCR_ANN_XOVR_99	Crossover code (Annual)
22	MSIS_TOS	MSIS Type of Service (TOS)
23	MSIS_TOP	MSIS Type of Program (TOP)
24	MAX_TOS	MAX Type of Service (TOS)
25	PRVDR_ID_NMBR	Billing provider identification number
26	NPI	National Provider Identifier
27	TAXONOMY	Provider Taxonomy
28	TYPE_CLM_CD	Type of claim
29	ADJUST_CD	Adjustment code
30	PHP_TYPE	Managed care type of plan code
31	PHP_ID	Managed care plan identification code
32	MDCD_PYMT_AMT	Medicaid payment amount
33	TP_PYMT_AMT	Third party payment amount
34	PYMT_DT	Payment/adjudication date
35	CHRG_AMT	Charge amount
36	PHP_VAL	Prepaid plan value
37	MDCR_COINSUR_PYMT_AMT	Medicare coinsurance payment amount
38	MDCR_DED_PYMT_AMT	Medicare deductible payment amount
39	ADMSN_DT	Admission date
40	SRVC_BGN_DT	Beginning date of service
41	SRVC_END_DT	Ending date of service
42	DIAG_CD_1	Principle Diagnosis code
43	DIAG_CD_2	Diagnosis codes (2nd diagnosis)
44	DIAG_CD_3	Diagnosis codes (3rd diagnosis)
45	DIAG_CD_4	Diagnosis codes (4th diagnosis)
46	DIAG_CD_5	Diagnosis codes (5th diagnosis)

47	MDCD_CVRD_MENTL_DAY_CNT	Mental hospital for the aged days
48	MDCD_CVRD_PSYCH_DAY_CNT	Inpatient Psychiatric (age < 21) days
49	INTRMDT_FAC_MR_DAY_CNT	ICF-MR days
50	NRSNG_FAC_DAY_CNT	Nursing facility days
51	LT_CARE_LVE_DAY_CNT	Leave days
52	PATIENT_STATUS_CD	Patient status
53	PATIENT_LIB_AMT	Patient liability amount

Medicaid Analytic Extract (MAX) Other Therapy File Variables

Column	Variable Name	Label
1	BENE_ID	Encrypted 723 CCW Beneficiary ID
2	MSIS_ID	Encrypted MSIS Identification Number
3	STATE_CD	State
4	YR_NUM	Year of MAX Record
5	EL_DOB	Birth date
6	EL_SEX_CD	Sex
7	EL_RACE_ETHNCY_CD	Race/ethnicity (from MSIS)
8	RACE_CODE_1	Race - White (from MSIS)
9	RACE_CODE_2	Race - Black (from MSIS)
10	RACE_CODE_3	Race - Am Indian/Alaskan (from MSIS)
11	RACE_CODE_4	Race - Asian (from MSIS)
12	RACE_CODE_5	Race - Hawaiian/Pac) Islands (from MSIS)
13	ETHNICITY_CODE	Ethnicity - Hispanic (from MSIS)
14	EL_SS_ELGBLTY_CD_LTST	State specific eligibility - most recent
15	EL_SS_ELGBLTY_CD_MO	State specific eligibility - mo of svc
16	EL_MAX_ELGBLTY_CD_LTST	MAX eligibility - most recent
17	EL_MAX_ELGBLTY_CD_MO	MAX eligibility - mo of svc
18	EL_MDCR_ANN_XOVR_OLD	Crossover code (Annual) old values
19	MSNG_ELG_DATA	Missing eligibility data
20	EL_MDCR_XOVR_CLM_BSD_CD	Crossover code (from claims only)
21	EL_MDCR_ANN_XOVR_99	Crossover code (Annual)
22	MSIS_TOS	MSIS Type of Service (TOS)
23	MSIS_TOP	MSIS Type of Program (TOP)
24	MAX_TOS	MAX Type of Service (TOS)
25	CLTC_FLAG	Community-based LT care (CLTC) flag
26	PRVDR_ID_NMBR	Billing provider identification number
27	NPI	National Provider Identifier
28	TAXONOMY	Provider Taxonomy
29	TYPE_CLM_CD	Type of claim
30	ADJUST_CD	Adjustment code
31	PHP_TYPE	Managed care type of plan code
32	PHP_ID	Managed care plan identification code
33	MDCD_PYMT_AMT	Medicaid payment amount
34	TP_PYMT_AMT	Third party payment amount
35	PYMT_DT	Payment/adjudication date
36	CHRG_AMT	Charge amount
37	PHP_VAL	Prepaid plan value
38	MDCR_COINSUR_PYMT_AMT	Medicare coinsurance payment amount
39	MDCR_DED_PYMT_AMT	Medicare deductible payment amount
40	SRVC_BGN_DT	Beginning date of service
41	SRVC_END_DT	Ending date of service
42	PRCDR_CD_SYS	Procedure (service) coding system
43	PRCDR_CD	Procedure (service) code
44	PRCDR_SRVC_MDFR_CD	Procedure (service) code modifier
45	DIAG_CD_1	Principle Diagnosis code
46	DIAG_CD_2	Diagnosis codes (2nd diagnosis)

47	QTY_SRVC_UNITS	Quantity of service
48	SRVC_PRVDR_ID_NMBR	Servicing provider identification number
49	SRVC_PRVDR_SPEC_CD	Servicing provider specialty code
50	PLC_OF_SRVC_CD	Place of service
51	UB_92_REV_CD	UB-92 revenue code
52	HCBS_TXNMY_WVR_CD	Home and Community-Based Services (HCBS)

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