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Quality of life and healthcare utilization and costs among adults with autism

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QUALITY OF LIFE AND HEALTHCARE UTILIZATION AND COSTS AMONG ADULTS WITH AUTISM

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ABSTRACT

OBJECTIVES

The objectives of this study are to: 1) assess construct validity of the World Health Organization's Quality of Life-BREF (WHOQOL-BREF) instrument, 2) evaluate quality of life (QOL) among adults with autism and 3) assess the prevalence, healthcare utilization and costs, and medication use among adults with autism enrolled in the Medicaid program.

METHODS

The study methodology included both primary and secondary data collection techniques. For objectives one and two, a cross-sectional, descriptive quantitative design was utilized. An internet-based survey using Qualtrics was administered to adults with autism enrolled with the Interactive Autism Network (IAN). The WHOQOL-BREF instrument was validated using confirmatory factor analysis (CFA). Structural equation modeling (SEM) was used to identify the factors influencing QOL among adults with autism. For objective three, a retrospective descriptive analysis of 2006-2008 Medicaid claims data for 39 states was conducted. Logistic regression was performed to assess trends in prevalence of autism and generalized linear mixed models (GLMM) were used to determine the predictors of healthcare utilization and costs among adults with autism.

RESULTS

The survey sample included 265 adults with autism. Based on the CFA analysis for objective one, the second-order hierarchical model of WHOQOL-BREF instrument was considered the

best fitting model among adults with autism. Results from the SEM analysis conducted under objective two revealed the modified Wilson and Cleary's QOL model tested in the study to have an adequate fit. Study results depicted autism severity (negative), maladaptive coping (negative), social support (positive) and functional independence (positive) as significant predictors of QOL. Study analyses under objective three highlighted a ~38% increase in the prevalence of autism from 2006 to 2008. Significant variation between demographic variables and healthcare expenditure and costs was observed after controlling for disease severity and other comorbid conditions.

CONCLUSIONS

Study results indicated that the WHOQOL-BREF is a psychometrically sound instrument to assess quality of life among adults with autism. Health care professionals involved in the management of autism among these adults should consider factors such as social support and coping when designing treatment strategies. With increasing prevalence, medical services as well as costs associated with management of adults with autism enrolled in the Medicaid program are likely to increase in the coming years.

DEDICATION

To My Husband

Maulik Parikh

LIST OF ABBREVIATIONS AND SYMBOLS

ADHD	Attention Deficit Hyperactivity Disorder
AQ	Autism Quotient
Brief-COPE	Brief Coping Orientation to Problem Experiences
CCI	Charlson Co-morbidity Index
CDC	Centers for Disease Control and Prevention
CFA	Confirmatory Factor Analysis
CFI	Comparative Fit Index
ER	Emergency room
FFS	Fee-for-Service
GLMM	Generalized Linear Mixed Model
HFA	High-Functioning Autism
HRQOL	Health-Related Quality of Life
IAN	Interactive Autism Network
ICD-9-CM	International Classification of Diseases, ninth revision, clinical modification
IFI	Incremental Fit Index
IRB	Institutional review board
IRR	incident rate ratio
ISEL-12	Interpersonal Support Evaluation List-12
MAX	Medicaid Analytic Extract

NNFI	Non-Normed Fit Index
PDD-NOS	Pervasive Developmental Disorder, Not Otherwise Specified
QOL	Quality of Life
RMSEA	Root mean square error of approximation
RUCA	Rural-urban commuting area codes
SAS	Statistical Analysis System
SEM	Structural Equation Modeling
SRMP	Root mean square residual
US	United States
WHO	World Health Organization
WHOQOL	World Health Organization Quality of Life

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TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

CHAPTER 1

INTRODUCTION

Autism spectrum disorders

Overview of autism

Autism spectrum disorders are neurodevelopmental disorders that are associated with significant impairment of social interaction and communication, and restricted and repetitive behavior (American Psychiatric Association, 2000). There are three types of autism: autistic disorder (also known as "classic" autism), Asperger syndrome and pervasive developmental disorder – not otherwise specified (PDD-NOS; known as "atypical autism"). Autistic disorder is the most severe form of autism, while Asperger syndrome and PDD-NOS are the milder forms of autism (CDC Website, 2015).

Etiology of autism

Genetic and environmental factors are believed to play a major role in the occurrence of autism (Newschaffer et al., 2007). The link between environmental exposures and autism is also plausible via gene-environment complex interaction; however, more research is currently being conducted to identify specific exposures associated with autism. Other potential risk factors and biomarkers of autism include infection and immune dysfunction, neurotransmitter, peptides and growth factors, endocrine factors, obstetric factors, xenobiotic factors, prescription medications (such as thalidomide, valproic acid, misoprostol), metals and other environmental exposures (Newschaffer, et al., 2007).

Prevalence of autism in adults

Although autism was initially considered a rare disorder affecting mainly children, evidence suggests that it is a lifelong disorder and it is a more common disorder than previously considered (Brugha et al., 2011; Newschaffer, et al., 2007). Prevalence of autism among children has significantly increased in the United States (US) in the past few decades (Boyle et

al., 2011). Possible reasons for rise in the prevalence rate are changes in screening and diagnostic criteria, increased awareness and knowledge among parents, healthcare professionals and society, and true increase in the prevalence rates (Wing & Potter, 2002). Currently, about 1 in 68 children have autism in the US (MMWR, 2014). Epidemiological data of adults with autism in the US is limited. One study has estimated the prevalence rate among adults with autism in England (Brugha, et al., 2011). Results from the study suggest that prevalence of autism in adults is similar to that in children (~1%). Prevalence rates were higher in males than females (Brugha, et al., 2011).

Healthcare utilization and costs associated with autism among adults

Past studies have highlighted a significant healthcare cost burden associated with autism. In a study of 2003 MarketScan data, Shimabukaro et al. (2007) reported a $4,690 incremental cost (~4 times higher) per year among privately insured individuals with autism aged 18-21 years compared to those without autism. The authors found that adolescent and children with autism incurred ~8-9.5 times greater median healthcare expenditure compared to children without the disorder. In their analysis of Mississippi Medicaid data, Khanna et al. (2013) fount that state Medicaid spent about $2 million for psychotropic drug costs among individuals with autism in 2007. Adults with autism were found to have the highest number of prescription claims with $3,391 average drug cost per recipient. In terms of hospitalization burden in the US, there were ~8,200 hospitalizations among adults with autism (>21 years) in 2007 (Lokhandwala, Khanna, & West-Strum, 2011). Past estimates suggest that the lifetime incremental societal direct and indirect cost of autism is $3.2 million where adult care (21%) and lost productivity (59.3%) account for the highest components of the total cost (Ganz, 2007). Based on recent estimates,

the direct and indirect economic burden of autism is ~$137 billion per year in the US (Autism Speaks 1, 2012).

Treatment of autism

Early diagnosis and treatment can help improve outcomes among individuals with autism. There are medical as well as nonmedical interventions and treatment options for individuals with autism beyond childhood. In general, the treatment options can be classified into behavioral therapies, pharmacological medicine, dietary approaches and complementary and alternative medicines (CDC Website, 2015). Interventions for adults with autism are mainly focused on providing better employment and living arrangements. For adolescents, apart from employment and living arrangements, additional training on vocational skills is provided (Volkmar, Cook, Pomeroy, Realmuto, & Tanguay, 1999). Currently, there is a lack of published literature on successful behavioral therapies among adults with autism (IAN Website, 2008). Most of the studies are restricted to children or young adolescent with autism. Based on the recently published meta-analysis of psychosocial interventions in adults with autism, only three types of interventions are studied in adults with autism (Bishop-Fitzpatrick, Minshew, & Eack, 2013). They include social cognition training, Applied Behavioral Analysis (ABA), and small community-based programs. ABA brings meaningful changes in behavior in terms of communication, social behavior, self-care, school and employment (CDC Website, 2015). Several studies confirm affirmative changes due to ABA in terms of employment and education in adolescent and young children with autism (Autims Speaks 2, 2015; IMPAQ International, 2010; Kasari & Lawton, 2010). There are several computer-based interventions available for adults with autism to address social deficits and communication (Bishop-Fitzpatrick, et al., 2013). In general, adults with autism with higher cognitive capabilities have seen better

improvements in employment and independent living due to the interventions (Volkmar, et al., 1999).

Currently there are no drugs available to cure autism. Pharmacotherapy is increasingly becoming the treatment mainstay. Antipsychotics such as risperidone and aripripazole are approved by the US Food and Drug Administration to treat severe tantrums, aggression and self-injurious behavior among children and adolescents with autism. Safety and efficacy of these agents are yet to be established in the adult population. It is unclear if the pharmacological treatments results among children can be generalized to adults with autism. A recent case series of adults with autism treated with aripriprazole may have had positive benefits in some patients (Jordan, Robertson, Catani, Craig, & Murphy, 2012). In the last few decades, there is an increase in off-label psychotropic medication use among individuals with autism, (Esbensen, Greenberg, Seltzer, & Aman, 2009; R. Khanna, et al., 2013) including adults. Complementary and alternative medicine (CAM) approaches are also becoming common among individuals with autism. However, there is a lack of well-documented benefit and safety profile of CAM among individuals with autism.

The concept of quality of life and health-related quality of life

Quality of life (QOL) is increasingly becoming an important treatment outcome in clinical trials, health care intervention and treatment, health surveys and epidemiological studies. Although many studies have used health-related quality of life (HRQOL) and QOL interchangeably, they are indeed very different concepts (Apolone & Mosconi, 1998; Feldman, Grundland, McCullough, & Wright, 2000; Patrick & Deyo, 1989). The World Health Organization defines QOL as "an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns." (WHOQoL Group, 1993). It is a broad construct that reflects an individual's physical, psychological, and social health, and its relationship with the environment. It encompasses health and non-health related domains including family life, environment, financing, housing, and other aspects of life. HRQOL, like subjective health status, is a part of overall QOL which reflects perceived health and well-being of an individual. HRQOL is referred to "the measure of the patients' functioning, well-being and general health perception in each of three domains: physical, psychological and social" (Apolone & Mosconi, 1998).

Types of quality of life measures

A good QOL measure should have a good discriminative power to differentiate between individuals with better and worse health (Guyatt, Feeny, & Patrick, 1993). Therefore, it is often suggested to test the validity, reliability, and responsiveness of generic or disease-specific instruments in the same (Patrick & Deyo, 1989) as well as different populations. There are two most common approaches to classify the QOL measures: generic measures and disease-specific (or condition-specific) measures (Dowie et al., 1998; Guyatt, et al., 1993; Patrick & Deyo, 1989). A key advantage of generic measures is that they are more general in nature and are broadly

applied to different disease states and conditions. However, they are often criticized as less "sensitive" and "responsive" to a specific disease state and hence often miss small but important changes in health (Guyatt, et al., 1993). Instead, disease-specific measures are more specific to the disease state (e.g., back pain or diabetes), certain function (sleep or emotional function) or special population (older adults or children with disability). They are often more responsive and clinically important to measure a specific aspect of the QOL in a particular patient. Generic measures are more often used because they allow comparison of different interventions and disease states (Patrick & Deyo, 1989). This information is useful for policy makers and other health care professionals to make important decisions, particularly in terms of resource allocation.

Generic instruments

Generic instruments include health profiles (36-item Short Form Health Survey, 12-item short form health survey version 2.0, sickness impact profiles, WHOQOL-BREF, etc.) and utility measures (EuroQol-5D, Health Utilities Index [HUI], Short Form-6 dimension [SF-6D], etc.). Health profiles usually measure all the aspects of health and are used across different demographics, irrespective of the disease state. Utility measures (also known as preference-based measures) mainly assess individuals' desire or preference for the condition or an outcome (Guyatt, et al., 1993; Torrance, 1987). Utility measures are derived from the modern utility theory and decision theory. A major advantage of utility measures is that they provide a utility score which is a single number on a continuum between 0.0 (death) and 1.0 (perfect health). Utilities form an underlying component in the assessment of quality-adjusted life-years (QALYs), which is often used in economic analysis to justify resources allocated to a particular treatment (Guyatt, et al., 1993; Torrance, 1987).

Quality of life among adults with autism

In recent years, QOL has emerged as a key outcome criterion to understand the physical and psychological impact of a disorder on an individual's well-being. Burgess and Gutstein (2007) suggested that studies should include social support, academic success, employment, and self-determination as key predictors of quality of life among adults with autism. However, to date, only a handful of studies have examined HRQOL or QOL among adults with autism. Majority of the studies have reported lower HRQOL or QOL among adults with autism (Billstedt, Gillberg, & Gillberg, 2011; Eaves & Ho, 2008; Jennes-Coussens, Magill-Evans, & Koning, 2006; Kamio, Inada, & Koyama, 2013; Kamp-Becker, Schroder, Remschmidt, & Bachmann, 2010; Rahul Khanna, Jariwala-Parikh, West-Strum, & Mahabaleshwarkar, 2014; Renty & Roeyers, 2006). Two studies have reported better QOL among adults with autism enrolled in behavioral treatment programs (Gerber, Baud, Giroud, & Galli Carminati, 2008; Persson, 2000).

According to a study by Renty and Roeyers, (2006) perceived informal social support was found to be a significant predictor of QOL among adults with high-functioning autism (HFA). However, the authors found no relationship between QOL and received informal and formal social support. Another study conducted by Kamp-Becker et al. (2010) reported lower HRQOL among adolescents and adults with HFA than the general population. Jennes-Coussens et al. (2006) also reported lower QOL, particularly physical and social domains, among patients with Asperger syndrome.

The most recent study conducted by Kamio et al. (2013) utilized a nationwide survey to assess predictors of QOL among adults with HFA. They reported lower psychosocial QOL among adults with HFA compared to general Japanese adults. Mothers' support and early diagnosis of the disease were associated with better QOL among adults. Aggressive behavior

was related to lower quality of life among adults. Two studies compared QOL among adults with autism to a disease reference group (Cottenceau et al., 2012; Kamp-Becker, et al., 2010). The results indicated that adults with autism have better QOL compared to schizophrenia patients (Kamp-Becker, et al., 2010), while another study found lower QOL compared to diabetes patients (Cottenceau, et al., 2012).

Study need

I. Need to test the psychometric properties of the health status instrument among adults with autism

There are two most common approaches to classify QOL instruments: generic instruments and disease-specific (or condition-specific) instruments (Dowie, et al., 1998; Guyatt, et al., 1993; Patrick & Deyo, 1989). Generic instruments are used to compare self-reported health status across different groups and disease conditions. Occasionally, the instruments are not reliable in certain subgroups such as elderly, low income, educated, different ethnic and cultural people. Therefore, in order to make the interpretation and comparison better, it is recommended that factorial validity and reliability of the instruments should be determined in different samples (Reed, 1998). Although past studies have used different QOL and HRQOL instruments to assess health status among adults with autism, none of the studies have tested the psychometric properties of the instruments.

Chapter 2 addresses the gap in literature by testing the psychometric properties of WHOQOL-BREF instrument among adults with autism. The WHOQOL-BREF instrument was initially developed to compare health status among individuals with different disease as well as different cultural origins (WHOQoL Group, 1993). Specifically, construct validity of the WHOQOL-BREF instrument was tested through confirmatory factor analysis and hypothesis testing. In addition, reliability and floor and ceiling effect of the WHOQOL-BREF instrument data is presented.

II. Need to evaluate quality of life (QOL) among adults with autism

As previously stated, autism is a developmental disorder that persists into adulthood (Brugha, et al., 2011; Newschaffer, et al., 2007). Despite an increasing amount of literature on predictors of outcomes in children with autism and their caregivers, very little is known about the outcomes in adults with autism. In addition, increase in the prevalence in adults with autism could impose significant humanistic and economic burden on the healthcare system (Piven & Rabins, 2011). One of the longest and largest prospective studies of a community sample of individuals with autism followed from childhood through adulthood reported worst psychosocial outcomes among adults with autism (Billstedt, Gillberg, & Gillberg, 2005).

Chapter 3 tests the relationship between autism severity, coping, functional independence, social support and quality of life in adults with autism. This study utilizes Wilson and Cleary's (1995) QOL model as a guiding framework. Certain modifications were made to Wilson and Cleary's QOL model to accommodate key constructs such as social support and coping that are essential in the context of the study. A cross-sectional descriptive design is used by conducting an online survey of these adults using the Qualtrics software program. Adults with autism registered with the Interactive Autism Network (IAN) were approached for the purpose of the study.

III. Need to assess autism prevalence, healthcare utilization and costs, and medication use among adults with autism enrolled in Medicaid.

With an increase in prevalence, there is an increase in the demand to support individuals with autism throughout their lifespan. It is essential to understand if adults with autism are receiving appropriate healthcare services. A study surveying physicians reported that physicians have not received adequate training to provide medical care to adults with autism (Bruder, Kerins,

Mazzarella, Sims, & Stein, 2012). Limited literature currently exists detailing autism-related utilization and costs for medical services and prescription drugs in adult population, particularly Medicaid beneficiaries. In addition, assessing the demographic variation in prevalence, incidence, costs, and resource utilization among adults with autism enrolled in Medicaid can help identify the need for targeting interventions in the US. For that purpose, in chapter 4, a retrospective analysis of the 2006-2008 Medicaid administrative claims data is conducted. Specifically, the trends in prevalence and medical services and prescription use were assessed. In addition, the predictors of healthcare utilization and costs among adults with autism in Medicaid are studied.

Specific aims and objectives

1. To test the psychometric properties of QOL instrument among adults with autism.
    a. Assess construct validity of the WHOQOL-BREF instrument.
    b. Assess the reliability and floor and ceiling effect of the WHOQOL BREF instrument.

2. To evaluate QOL among adults with autism.
    a. Determine QOL among adults with autism in the United States.
    b. Identify the determinants of QOL among adults with autism by using a modified version of the Wilson and Cleary's QOL conceptual model to study the relationship between autism severity, coping, functional independence, social support and quality of life in adults with autism.

3. To study the prevalence, healthcare utilization and costs, and medication use among adults with autism enrolled in the Medicaid program (national data).
    a. Estimate the trends in i) autism prevalence and ii) autism-related medical services and prescription use.
    b. Assess the predictors of healthcare utilization and costs among adults with autism in Medicaid.

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CHAPTER 2

PSYCHOMETRIC PROPERTIES OF WHOQOL-BREF INSTRUMENT AMONG ADULTS WITH AUTISM

INTRODUCTION

Autism spectrum disorders are neurodevelopmental disorders that are associated with limited social development, behavioral and language skills. Over the last few decades, there has been a substantial increase in the prevalence rate of autism in the United Stated (US) (CDC Website, 2015). Current estimates suggest that 1 in every 68 (~1.47%) children in the US has autism (MMWR, 2014). Prevalence rate of autism among adults is currently unknown in the US; however, based on the study conducted in England, the rate among adults has been found to be similar to those among children (~1%; Bruga et al., 2011).

Quality of life (QOL) signifies an individual's perception of their position in life and the role of culture and value systems in influencing those perceptions. Besides including health (physical, psychological, and social) related domains, QOL also encompasses non-health (political, environmental) related domains (WHOQoL Group, 1993). There are several generic and disease-specific instruments available to measure QOL. The merit of the use of generic instrument is the ability to compare QOL among different population and disease condition (Guyatt, Feeny, & Patrick, 1993). The World Health Organization's Quality of Life-100 (WHOQOL-100), developed by World Health Organization (WHO), is the most commonly and widely used generic QOL instrument. This generic instrument has more than 20 international versions and cross-cultural adaptations making it convenient to compare patients with different disease conditions and different cultures. In order to reduce respondent burden, WHOQOL-BREF, an abbreviated version of the WHOQOL-100 instrument was developed (Skevington, Lotfy, & O'Connell, 2004). WHOQOL-BREF contains 26-items including one item on the 24

facets of QOL, one item assessing overall QOL, and one item assessing general health. The 24-items are measured on a five-point scale. Four broad domains consist of: physical health (seven items), psychological health (six items), social relationships (three items) and environment (eight items).

Results from the first international field trial conducted in 23 countries (n=11,830) indicated that the WHOQOL-BREF had excellent to good validity and reliability (Skevington, et al., 2004). The instrument has been validated among general population in different countries including US (Colbourn, Masache, & Skordis-Worrall, 2012; Hanestad, Rustoen, Knudsen, Lerdal, & Wahl, 2004; Jaracz, Kalfoss, Gorna, & Baczyk, 2006; Li, Kay, & Nokkaew, 2008; Nedjat, Montazeri, Holakouie, Mohammad, & Majdzadeh, 2008; Usefy et al., 2010; Xia, Li, Hau, Liu, & Lu, 2012; Yao, Chung, Yu, & Wang, 2002) as well as diseased population such as pulmonary tuberculosis, disability students, physical impairments traumatic brain injury, depression, traumatic spinal-cord injury, psychiatric adult population, rheumatoid arthritis and others (Bandar, Jani, & Karim, 2014; Berlim, Pavanello, Caldieraro, & Fleck, 2005; Chiu et al., 2006; Chung, Lan, & Yang, 2012; Jang, Hsieh, Wang, & Wu, 2004; Kim, Hahn, Im, & Yang, 2013; Masthoff, Trompenaars, Van Heck, Hodiamont, & De Vries, 2005; Miller, Chan, Ferrin, Lin, & Chan, 2008; W. J. Taylor, Myers, Simpson, McPherson, & Weatherall, 2004; Trompenaars, Masthoff, Van Heck, Hodiamont, & De Vries, 2005). The results of these past studies suggest that the WHOQOL-BREF instrument possesses good psychometric properties. The four-factor hierarchical model, where second-order factor (QOL) had a direct influence on first-order factors (physical, psychological, social and environment) has been reported to have a better fit compared to other one-factor models (Masthoff, et al., 2005; Miller, et al., 2008; Skevington, et al., 2004; Xia, et al., 2012; Yao, et al., 2002). The instrument also been shown to

demonstrate reasonable known-groups validity and reliability in diverse disease population (Jang, et al., 2004; Jaracz, et al., 2006; Kim, et al., 2013; Skevington, et al., 2004; Xia, et al., 2012; Yao, et al., 2002).

Although WHOQOL-BREF instrument has been previously used to assess QOL among adults with autism (Jennes-Coussens, Magill-Evans, & Koning, 2006; Kamio, Inada, & Koyama, 2013; Kamp-Becker, Schroder, Remschmidt, & Bachmann, 2010), its psychometric properties for independent use in this population is not yet tested. An instrument like WHOQOL-BREF that has been developed for a general population may not hold its psychometric profile in a disease population. Therefore, it is often suggested to test the validity, reliability, and responsiveness of generic or disease-specific instruments in the same (Patrick & Deyo, 1989) as well as different populations. The purpose of this study was to assess the construct validity (factorial validity, convergent validity, discriminant validity and known-groups validity), reliability (internal consistency) and floor and ceiling effect of WHOQOL-BREF instrument among adults with autism spectrum disorders.

METHODS

Study sample and procedure

A cross-sectional study using an Internet-based survey of adults with autism enrolled at Interactive Autism Network (IAN) was performed using Qualtrics survey software program. IAN, operated by Kennedy Krieger Institute, is the largest online research-based registry of adults and children with autism and their caregivers in the US. The cover letter explaining the purpose of the study, eligibility criteria, contact information and study link was emailed to the participants. The respondents eligible for the study were required to be at least 18 years of age. In addition, it was required that they could respond to the question with little or no proxy help. Study approval was obtained from the University of Mississippi Institutional Review Board (UM IRB) under exempt status.

This study is part of a bigger research study among adults with autism; however, only information applicable to this study has been reported in this chapter. The survey included two sections. Section I included four measures: WHOQOL-BREF, Brief Coping Orientation to Problem Experiences (Brief-COPE; coping instrument), Interpersonal Support Evaluation List-12 (ISEL-12; social support instrument), Waisman Activities of Daily Living Scale (functional independence instrument) and Autism-Quotient 10 (AQ-10; autism severity instrument). Section II will include sociodemographic questions. The survey was open for a period of month between August 29, 2013 and September 19, 2013. Survey respondents were assured confidentiality of

responses and data anonymity. A $5 incentive (Amazon gift-card) for participation was provided to the study participants.

Measures

Quality of life

WHOQOL-BREF contains 26-items, including one item on overall QOL and one item on general health (Skevington, et al., 2004). The remaining 24-items are measured on a five-point scale classified into four domains: physical health (seven items), psychological health (six items), social relationships (three items) and environment (eight items). There are three reversed coded items in the questionnaire. The raw scores for each domain were calculated by adding the scores of the item in each domain. The raw scores were further transformed to 0-100 by using an algorithm provided by the WHOQOL-BREF group (World Health Organization, 1996). Lower score indicate poor QOL.

Autism severity

AQ-10 is a self-reported shorter version of the 50-item parent version AQ (Allison, Auyeung, & Baron-Cohen, 2012). The 10-item AQ is measured on a four-point Likert scale (strongly agree, slightly agree, slightly disagree, strongly disagree). The instrument captures severity in five domains including social interaction, communication, attention to detail, attention switching and imagination. A total score is assessed by summing score on all the items, with higher score indicating greater severity of autistic behavior. Based on a cut-off value of six, individuals can be classified into low and high severity (Allison, et al., 2012).

Analysis

Items distribution and quality

Descriptive statistics including mean, standard deviation (SD), median, and missing data (%) were reported. Kurtosis and skew coefficients were calculated to check for normality. The absolute value greater than 1.0 indicates problems with the distribution.

Construct validity

Correlation analyses

WHOQOL-BREF domain to domain correlation was performed using Pearson correlation coefficient. Correlation between WHOQOL-BREF items with the domains as well overall QOL and general health item was also reported using Pearson correlation coefficient. In order to establish validity of WHOQOL-BREF instrument, the association of each domain with respect to general health and overall QOL was assessed using linear regression.

Convergent and discriminant analyses

Convergent and discriminant validity of WHOQOL-BREF was determined by testing several relationships using corrected item-total correlation and item-to-other scale correlation. For convergent validity, the expected items in the same domain should correlate strongly with each other compared to the items from other domains. For discriminant validity, the items from different domains should have a low or no correlation with each other. Convergent and discriminant validity was demonstrated by examining corrected item-total correlation between individual items in a domain with total score of the remaining items in the same or other domains. The corrected-item total correlation should be higher for similar domains compared to corresponding domains (at least ≥ 0.40) to demonstrate convergent validity. For discriminant validity, the corrected item-to-other scale correlation should be lower for unrelated domains.

Confirmatory factor analysis

Hypothetical structure of the WHOQOL-BREF instrument was validated using confirmatory factor analysis (CFA). The assumptions of multivariate normality and linearity were evaluated by checking significance in skew and kurtosis index (Harrington, 2008; Kline, 2010). The model's fit was determined using different fit indices (Harrington, 2008; Kline, 2010; Schreiber, Nora, Stage, Barlow, & King, 2006). Most common fit indices are Normed Fit Index (NFI), Non-Normed Fit Index (NNFI, also known as TLI), Incremental Fit Index (IFI), Comparative Fit Index (CFI), root mean square error of approximation (RMSEA) and root mean square residual (SRMR). The criteria suggested for good fit of the model are NFI>.90, TLI>.95, IFI>.90, CFI>.95, RMSEA<.06 and SRMR<.08. Similar to the studies in the past, the most commonly tested CFA models were compared in this study: one factor model and second-order model (Masthoff, et al., 2005; Miller, et al., 2008; Skevington, et al., 2004; Xia, et al., 2012; Yao, et al., 2002). For one-factor model, all the items are said to have a direct effect on QOL. For the second model (Figure 2.1), the second-order factor (QOL) is said to have a direct effect on each first-order factor (physical, psychological, social relationship and environment). In order to determine which model fits the data best, akaike information criteria (AIC; smaller is better) fit indices were calculated for nested models (Kline, 2010). CFA was conducted using IBM SPSS AMOS 22.0 (IBM Corporation, Armonk, NY, US) statistical software.

Known-groups validity

The most important factor to consider when validating a QOL questionnaire is whether it can discriminate between different levels of disease severity. A cut-off of six was used to differentiate between high and low levels of severity groups (Allison, et al., 2012). Independent

sample t-test was conducted to test whether the WHOQOL-BREF instrument can discriminate between different levels of autism severity.

Reliability

The internal reliability of WHOQOL-BREF was assessed by means of Cronbach's coefficient alpha. Internal consistency reliability ≥0.70 is considered adequate, with values ≥0.80 considered preferable (Gliem & Gliem, 2003; Nunnally & Bernstein, 1994).

Floor and ceiling effect

The floor effect was determined by calculating the percentage of respondents selecting the lowest possible score on a five-point scale of each item. The ceiling effect is determined by calculating the percentage of people choosing the highest possible score on a five-point scale of an item. The following criteria for floor and ceiling effects were used: no floor or ceiling effect (excellent); floor or ceiling effect ≤20% (adequate) and floor or ceiling effect ≥20% (poor) (McHorney & Tarlov, 1995).

RESULTS

Socio-demographic characteristics

The final study sample consisted of 265 adults with autism (Table 2.1). Majority of the study participants were male (56%), white (83%), and had a mean age of 33.1 (±13.76) years. Around 63% had a diagnosis of Aspergers syndrome followed by classic autism (~22%) and PDD-NOS (~13%). Participants also reported having other mental (48.1%) and physical illnesses (~41%) besides being diagnosed with autism.

Table 2.1: Study sample characteristics (N=265)

Characteristic	**N (%)**
Age (in years), Mean (SD)	33.08 (±13.76)
Male, N (%)	147 (55.7)
White, N (%)	218 (82.6)
Insurance status, N (%)	
Public	112 (42.4)
Private including HMO	120 (45.5)
No insurance	30 (11.4)
Residential Status, N (%)	
Living independently	77 (29.2)
Living with a partner	55 (20.8)
Living with family	120 (45.5)
Living in a supported home (group home)	10 (3.8)
Primary diagnosis, N (%)	
Classic autism/autistic disorder	59 (22.3)
Asperger's syndrome	166 (62.9)
PDD-NOS	35 (13.3)
Occupation	
Employed/Self-employed full-time	62 (23.5)
Employed part-time	39 (14.8)
Student	54 (20.5)
Seeking work	39 (14.8)

Other	70 (26.5)
Other physical illness (yes), N (%)	108 (40.9)
Other mental illness (yes), N (%)	127 (48.1)
PDD-NOS, Pervasive Developmental Disorder, Not Otherwise Specified	

Items distribution and quality

The mean score, kurtosis and skewness coefficients and missing data on the WHOQOL-BREF items were assessed (Table 2.2). Mean scores of all 26 items of WHOQOL-BREF ranged from 2.70 (±1.23; item 21) to 3.82 (±1.01; item 15) on a 5-point response scale. The mean score and the SD of the individual domains were 58.90 (±18.26) for physical health, 54.59 (±16.98) for psychological health, 48.26 (±23.29) for social relationships and 58.12 (±17.96) for environment domain. Majority of the WHOQOL-BREF items have kurtosis and skewness coefficient within the acceptable range of -1.00 to 1.00. Three items were slightly outside the range for kurtosis coefficient but still less than 1.11. Based on the ranges, the data appeared to be normally distributed. Total missing data was around 3.7% (total items) with 0.0%-0.7% missing data on individual items. No items were deleted because we had minimal missing data (<20%) (World Health Organization, 1996). Mean-substitution was used to replace item scores where there was only one item missing within a domain. Only one respondent had more than 2 items missing for the same domain (environment). For that respondent, the domain score was not calculated.

Table 2.2: Summary statistic of the WHOQOL-BREF instrument							
Items*	**Mean (SD)**	**Median**	**Missing**	**Skewness**	**Kurtosis**	**Floor (%)**	**Ceiling (%)**
Overall QOL (item 1)	3.63 (0.89)	4	0.00%	-0.395	-0.389	0.4	14.0
General health (item 2)	3.18 (1.04)	3	0.00%	-0.095	-0.941	3.4	8.3
Pain (item 3)	3.71 (1.10)	4	0.00%	-0.448	-0.743	29.2	2.3
Medication (item 4)	3.49 (1.16)	4	0.00%	-0.359	-0.773	22.3	5.3
Positive feeling (item 5)	3.40 (0.93)	3	0.00%	-0.18	-0.339	1.9	10.6
Spirituality (item 6)	3.21 (1.01)	3	0.38%	-0.278	-0.441	5.3	8.0
Think (item 7)	3.16 (0.95)	3	0.38%	-0.062	-0.402	3.4	7.2
Safety (item 8)	3.53 (0.93)	4	0.38%	-0.563	0.002	2.3	11.4
Environment (item 9)	3.55 (0.93)	4	0.38%	-0.424	0.002	2.3	13.6
Energy (item 10)	3.10 (0.95)	3	0.00%	-0.205	-0.35	4.9	4.9
Body (item 11)	3.08 (1.04)	3	0.00%	-0.283	-0.651	7.6	5.3
Finance (item 12)	2.72 (1.20)	3	0.38%	0.12	-0.944	19.3	6.8
Information (item 13)	3.45 (0.98)	4	0.00%	-0.426	-0.284	3.0	12.1
Leisure (item 14)	3.25 (1.12)	3	0.38%	-0.11	-0.83	5.3	14.4
Mobility (item 15)	3.82 (1.01)	4	0.00%	-0.54	-0.473	1.1	29.2
Sleep (item 16)	3.00 (1.19)	3	0.00%	-0.178	-1.114	12.1	7.2
Activities (item 17)	3.31 (1.05)	3	0.00%	-0.337	-0.628	4.5	10.2
Work (item 18)	3.09 (1.27)	3	0.00%	-0.071	-1.118	12.1	15.5
Esteem (item 19)	3.35 (1.10)	3	0.38%	-0.255	-0.763	4.5	14.8
Relationship (item 20)	2.99 (1.15)	3	0.00%	-0.18	-0.971	11.7	6.8
Sex (item 21)	2.70 (1.23)	3	0.75%	0.102	-0.877	23.1	8.3
Support (item 22)	3.10 (1.10)	3	0.00%	-0.203	-0.619	9.1	9.1
Home (item 23)	3.29 (1.21)	3	0.38%	-0.182	-1.076	6.4	18.2
Services (item 24)	3.29 (1.15)	3	0.00%	-0.26	-0.897	6.1	14
Transportation (item 25)	3.53 (1.16)	4	0.00%	-0.597	-0.391	7.2	20.8
Negative feeling (item 26)	2.92 (1.00)	3	0.00%	-0.198	-0.628	3.0	9.1
SD, Standard deviation; WHOQOL, World Health Organization Quality of Life *** Items are measured on 5-point response scale**							

Construct validity

Correlation analyses

Domain to domain correlations

Pearson Correlations between WHOQOL-BREF domains ranged from 0.332 between social relationship and physical health to 0.662 between physical health and environment (Table 2.3).

Table 2.3: Inter-correlation of the WHOQOL-BREF domains

	Physical Health	**Psychological Health**	**Social Relationships**	**Environment**
Psychological Health	.594**			
Social Relationships	.332**	.550**		
Environment	.622**	.615**	.441**	

WHOQOL, World Health Organization Quality of Life
****correlation significant at *p<0.001* level**

Item to domain correlations

The strength of association between corresponding domains, general health item and overall QOL items with individual items were assessed using Pearson correlation (Table 2.4). Correlation coefficients ranged from r=0.168 to r=0.761 for physical domain, r=0.242 to r=0.724 for psychological domain, r=0.122 to r=0.835 for social relationships domain, r=0.218 to r=0.739 for environment domain, r=0.244 to r=0.510 for overall QOL item and r=0.176 to r=0.475 for general health item. None of the items had a stronger correlation with other corresponding domains compared to its original domain.

Table 2.4: Item-to-domain inter-correlations of the WHOQOL-BREF						
	Overall QOL (item 1)	**General health (item 2)**	**Physical health**	**Psychological health**	**Social Relationships**	**Environment**
Pain (item 3)	0.340**	0.475**	0.659**	0.242**	0.122*	0.341**
Medication (item 4)	0.298**	0.464**	0.642**	0.247**	0.146*	0.267**
Positive feeling (item 5)	0.421**	0.284**	0.383**	0.709**	0.369**	0.387**
Spirituality (item 6)	0.430**	0.312**	0.383**	0.724**	0.361**	0.445**
Think (item 7)	0.264**	0.271**	0.360**	0.611**	0.286**	0.356**
Safety (item 8)	0.419**	0.252**	0.400**	0.384**	0.162**	0.649**
Environment (item 9)	0.383**	0.396**	0.505**	0.463**	0.281**	0.597**
Energy (item 10)	0.370**	0.460**	0.689**	0.508**	0.281**	0.432**
Body (item 11)	0.304**	0.386**	0.422**	0.634**	0.420**	0.424**
Finance (item 12)	0.402**	0.257**	0.348**	0.419**	0.359**	0.625**
Information (item 13)	0.457**	0.336**	0.464**	0.466**	0.367**	0.730**
Leisure (item 14)	0.387**	0.288**	0.388**	0.386**	0.325**	0.659**
Mobility (item 15)	0.360**	0.345**	0.584**	0.274**	0.191**	0.459**
Sleep (item 16)	0.299**	0.367**	0.600**	0.415**	0.232**	0.397**
Activities (item 17)	0.510**	0.420**	0.761**	0.561**	0.307**	0.573**
Work (item 18)	0.345**	0.438**	0.699**	0.506**	0.267**	0.435**
Esteem (item 19)	0.376**	0.373**	0.462**	0.690**	0.350**	0.435**
Relationship (item 20)	0.398**	0.310**	0.306**	0.507**	0.835**	0.408**
Sex (item 21)	0.244**	0.176**	0.168**	0.351**	0.812**	0.218**
Support (item 22)	0.428**	0.254**	0.336**	0.474**	0.759**	0.449**
Home (item 23)	0.404**	0.250**	0.422**	0.388**	0.309**	0.676**
Services (item 24)	0.458**	0.313**	0.456**	0.414**	0.267**	0.739**
Transportation (item 25)	0.327**	0.227**	0.345**	0.359**	0.251**	0.627**
Negative feeling (item 26)	0.401**	0.341**	0.391**	0.693**	0.444**	0.444**
WHOQOL, World Health Organization Quality of Life ****correlation significant at *p<0.01* level; *correlation significant at *p<0.05* level**						

Convergent and discriminant validity

Corrected item-total correlation and item-to-other scale correlation was calculated in order to demonstrate convergent and discriminant validity of WHOQOL-BREF instrument (Table 2.5). Corrected item-total correlation ranged from 0.420 to 0.652 for physical health, 0.431 to 0.562 for physiological health, 0.489 to 0.608 for social relationships and 0.471 to 0.633 for environment domain. The correlation of the items with their own domain was found to be at least 0.40 suggesting acceptable convergent validity. For majority of items, item-to-other scale correlation (discriminant validity) was found to be lower than 0.40. Item-to-other scale correlation for physical health ranged from 0.362 to 0.459 with physiological health, 0.169 to 0.38 with social relationships and 0.341 to 0.505 with environment domain, respectively. For other domains, in general, the item-to-other scale coefficient ranged from 0.245 (item 3; physical health) to 0.562 (item 17; physical health) for physiological health, 0.124 (item 3; physical health) to 0.442 (item 26; physiological health) for social relationships and 0.218 (item 21; social relationships) to 0.573 (item 17; physical health) for environment domain supporting discriminant validity for the instrument.

Table 2.5: Convergent and discriminant validity for WHOQOL-BREF items				
	Physical Health	**Psychological Health**	**Social Relationships**	**Environment**
Physical health				
Pain (item 3)	**0.510**	0.245	0.124	0.341
Medication (item 4)	**0.478**	0.250	0.147	0.267
Energy (item 10)	**0.572**	0.509	0.282	0.432
Mobility (item 15)	**0.430**	0.274	0.191	*0.459**
Sleep (item 16)	**0.420**	0.416	0.233	0.397
Activities (item 17)	**0.652**	0.562	0.307	0.573
Work (item 18)	**0.533**	0.507	0.268	0.435
Psychological health				
Positive feeling (item 5)	0.388	**0.563**	0.369	0.387
Spirituality (item 6)	0.386	**0.569**	0.362	0.445
Esteem (item 19)	0.459	**0.499**	0.350	0.435
Think (item 7)	0.362	**0.431**	0.287	0.356
Body (item 11)	0.424	**0.441**	0.421	0.424
Negative feeling (item 26)	0.385	**0.522**	0.442	0.444
Social relationships				
Relationship (item 20)	0.305	0.507	**0.608**	0.408
Sex (item 21)	0.169	0.351	**0.538**	0.218
Support (item 22)	0.338	0.475	**0.489**	0.449
Environment				
Safety (item 8)	0.400	0.384	0.162	**0.540**
Environment (item 9)	*0.505**	0.463	0.281	**0.478**
Finance (item 12)	0.348	0.420	0.359	**0.471**
Information (item 13)	0.465	0.467	0.368	**0.633**
Leisure (item 14)	0.390	0.387	0.326	**0.526**
Home (item 23)	0.423	0.389	0.309	**0.534**
Services (item 24)	0.457	0.415	0.267	**0.624**
Transportation (item 25)	0.341	0.357	0.250	**0.480**

WHOQOL, World Health Organization Quality of Life
Values are based on corrected total-item correlation
Bold font highlights the corrected total-item correlation with its own domain.
***Italics font suggests the highest corrected total-item correlation with other domain**

Association of domains with general facet items

In order to establish construct validity of WHOQOL-BREF instrument, the association of each domain with respect to overall QOL and general health was also assessed (Table 2.6). The overall QOL was strongly associated with environment and psychological domains whereas general health was strongly associated with physical health domain. The contribution of domain score on overall QOL and general health was also studied using multiple regression. For overall QOL item, physical, social relationships and environment domains had significantly positive contribution after controlling for other variables ($p<0.01$). Roughly 44% (adjusted r^2) of variance on overall QOL was explained by the underlying domains. Physical health (β=0.031; $p<0.001$) and psychological health (β=0.009; $p=0.035$) have significantly predictive effect on general health item after controlling for other variables. The variance explained by all the domains on the general health was around 42% (adjusted r^2).

Table 2.6: Regression analysis and correlation of WHOQOL-BREF domains with general facet items

	Adjusted R2		**Physical Health**	**Psychological Health**	**Social Relationships**	**Environment**
Overall QOL	0.44	**Correlation**	0.536**	0.540**	0.439**	0.609**
		B	0.010**	0.007	0.006**	0.014**
General Health	0.42	**Correlation**	0.638**	0.486**	0.304**	0.432**
		B	0.031**	0.009*	0.002	-0.001

WHOQOL, World Health Organization Quality of Life
*****p<0.05***
β values are based on linear regression

Confirmatory factor analysis

Tables 2.7 and 2.8 summarize the results from CFA analysis for the two models tested. Comparison was made between one-factor model and a four-factor hierarchical model. A poor

fit was observed for the one-factor model (Chi-square[df] =766.37[252], *p<0.05*; GFI=0.792; AGFI=0.752, CFI=0.752 and RMSEA=0.08 [0.081-0.095]). The second-factor model fit was found to be comparatively good: Chi-square(df) =575.35 (248), *p<0.05*; GFI=0.847; AGFI=0.841, CFI=0.842 and RMSEA=0.071 (0.063-0.078). Based on the modification indices, six pairs of items were correlated in the second factor model. The model fit improved substantially when error terms for items 3 and 4, items 5 and 6, items 9 and 10, items 18 and 19, items 9 and 23 and items 15 and 25 were covaried. The model fit of the of the final model improved significantly: Chi-square(df) =428.00 (242), *p<0.05*; GFI=0.885; AGFI=0.858, CFI=0.885 and RMSEA=0.054 (0.046-0.062). The final model is depicted in Figure 2.1. The revised hierarchical second-order model was more parsimonious and represented a significantly better fit compared to hierarchical second-order factor and first-order factor model (χ^2 difference =191.02, df=4; *p<0.001*). In the final modified model, factor loadings of all the items on their corresponding domains as well first-order factor loadings on QOL (second-order factor) were found significant (*p<0.001*; Table 2.8).

Table 2.7: Goodness to fit for confirmatory factor analysis analyses for WHOQOL-BREF instrument

	First-order model	**Four second-order hierarchical model**
Chi-square (DF)	766.37 (252)***	428.002 (242)***
CFI (>0.90)	0.752	0.91
GFI (>0.90)	0.792	0.885
AGFI (>0.80)	0.752	0.858
RMSEA (0.06-1)	0.08 (0.081-0.095)	0.054 (0.046-0.062)
AIC (smaller is better)	862.366	544.002

WHOQOL, World Health Organization Quality of Life
******p<0.001***

Table 2.8: Unstandardized estimation of four second-order hierarchical model				
	First-order factor loading		**Second-order factor loading**	
	Estimation (SE)	**R^2**	**Estimation (SE)**	**R^2**
Physical health			1.000	0.702
Pain (item 3)	0.586 (0.090)	0.206		
Medication (item 4)	0.565 (0.094)	0.172		
Energy (item 10)	0.693 (0.078)	0.402		
Mobility (item 15)	0.565 (0.082)	0.229		
Sleep (item 16)	0.745 (0.098)	0.287		
Activities (item 17)	0.973 (0.092)	0.631		
Work (item 18)	1.000	0.45		
Psychological health			0.851 (0.111)	0.942
Positive feeling (item 5)	0.841 (0.110)	0.326		
Spirituality (item 6)	0.947 (0.121)	0.347		
Esteem (item 19)	0.745 (0.110)	0.371		
Think (item 7)	0.958 (0.123)	0.242		
Body (item 11)	1.071 (0.132)	0.336		
Negative feeling (item 26)	1.000	0.393		
Social relationships			0.707 (0.107)	0.488
Relationship (item 20)	1.240 (0.141)	0.605		
Sex (item 21)	1.045 (0.133)	0.378		
Support (item 22)	1.000	0.434		
Environment			0.717 (0.108	0.724
Safety (item 8)	0.896 (0.128)	0.34		
Environment (item 9)	0.816 (0.124)	0.281		
Finance (item 12)	1.103 (0.163)	0.308		
Information (item 13)	1.162 (0.148)	0.509		
Leisure (item 14)	1.135 (0.158)	0.374		
Home (item 23)	1.145 (0.167)	0.324		
Services (item 24)	1.306 (0.170)	0.471		
Transportation (item 25)	1.000	0.276		

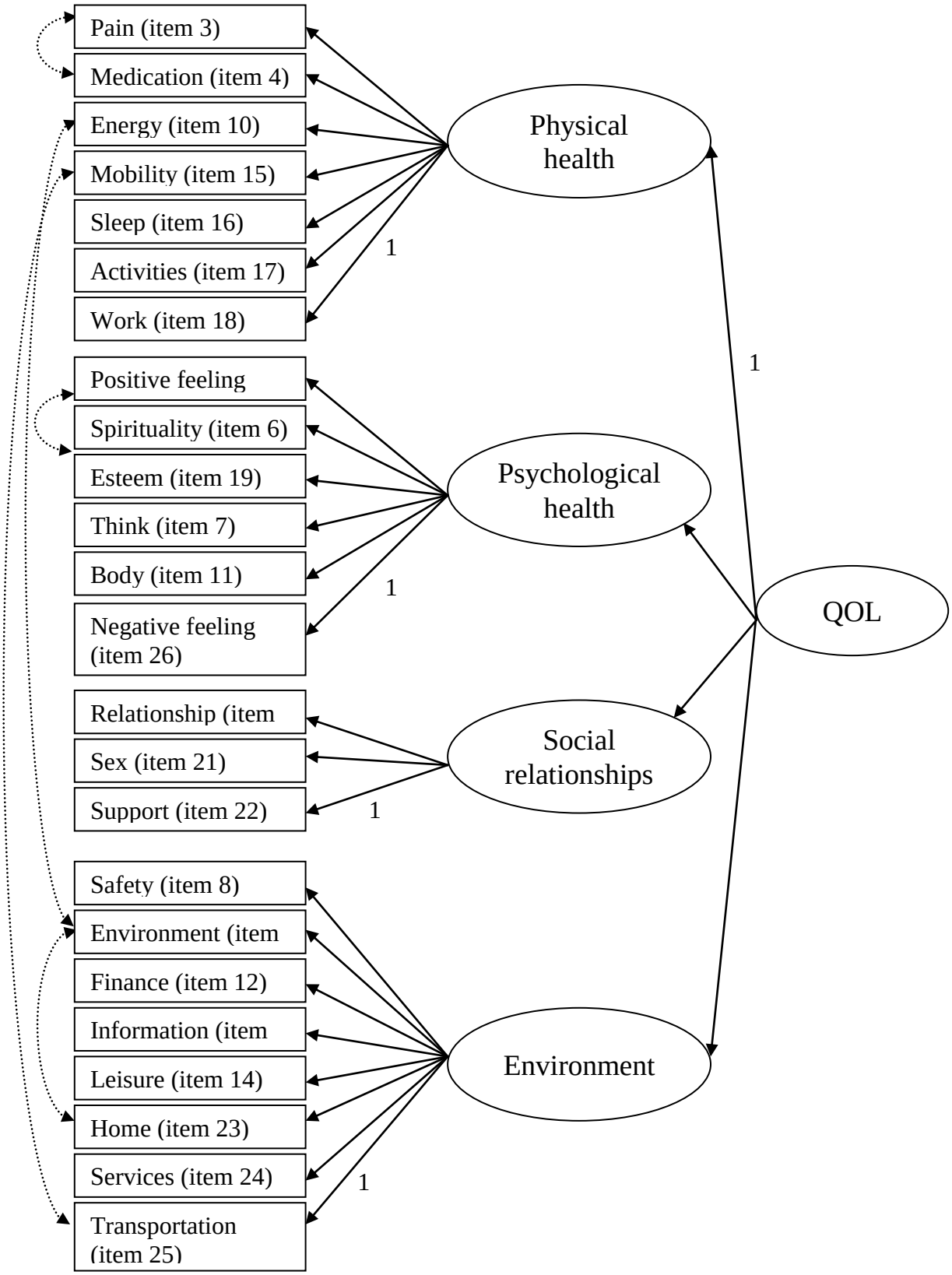

Figure 2.1: Confirmatory factor analysis on the second-order factor

Known-groups validity

The ability of the WHOQOL-BREF instrument to discriminate between low and high severity groups was tested using the independent sample t-test (Table 2.9). The mean scores were significantly higher for group 1 (low severity) compared to group 2 (high severity) for physical health (61.2±18.1 *vs.* 56.8±18.0; *p=0.03*) and physiological (58.3±15.8 *vs.* 51.6±17.5; *p=0.002*) health domains. There was no significant difference in social relationships and environment domains scores between low and high autism severity groups (*p>0.05*).

Table 2.9: Known-groups validity for the WHOQOL-BREF domains

	Autism Severity		***p value***
Domains	**Low severity (N=116)**	**High severity (N=143)**	
Physical health	61.70 (18.07)	56.77 (18.03)	0.030
Psychological health	58.26 (15.80)	51.60 (17.45)	0.002
Social Relationships	50.00 (22.74)	46.97 (23.83)	0.300
Environment	60.16 (16.53)	56.75 (19.15)	0.132

WHOQOL, World Health Organization Quality of Life
Values are presented as mean (standard deviation)
***P values* are based on independent t-test**

Internal consistency

The overall Cronbach's alpha was found to be 0.914 for 26 items (Table 2.10). Cronbach's alpha for individual domains were 0.784 for physical health (7 items), 0.761 for psychological health (6 items), 0.722 for social relationships (3 items) and 0.815 for environment (8 items), respectively. The corrected-item correlation was also found to be within the range (0.430-0.651), suggesting that the items have good correlation with the other items in the same domain.

Table 2.10: Reliability for the WHOQOL-BREF domains			
	Mean (SD)	**Cronbach's Alpha**	**No. of items**
Physical health	58.90 (18.26)	0.784	7
Psychological health	54.59 (16.98)	0.761	6
Social relationships	48.26 (23.29)	0.722	3
Environment	58.12 (17.96)	0.815	8
Overall	-	0.914	26
WHOQOL, World Health Organization Quality of Life			

Floor and ceiling effect

Table 2.2 displays the results for floor and ceiling effects. The floor and ceiling effects were non-existent with the exception of three items which displayed floor effects (items 3, 4 and 21) and two items which displayed ceiling effects (items 15 and 25).

DISCUSSION

Though a few studies have used the WHOQOL BREF to assess QOL among adults with autism, the psychometric properties of this instrument in this population remains unknown. To the best of our knowledge, this is the first study to assess psychometric properties of WHOQOL-BREF instrument among adults with autism. Study results depicted acceptable construct validity and know-group validity of WHOQOL-BREF instrument in this population. The reliability of the instrument was also found to be reasonable. Floor and ceiling effects were limited.

Domain structure and distribution of WHOQOL-BREF scores

Majority of participants reported good overall QOL and were on average satisfied with their health. With respect to individual domain scores, the mean score for physical health was 58.90 (±18.26), psychological health was 54.59 (±16.98), social relationships was 48.26 (±23.29) and environment was 58.12 (±17.96). The participants reported more than average scores for vast majority of items as well as all domains. This suggests that overall, adults with autism valued their QOL in a positive direction. The mean score for item 12, which is regarding having enough money to meet their needs, was 2.72. This is understandable because individuals with autism struggle to be independent and do not have a suitable source of employment (Hendricks, 2010; J. Taylor & Seltzer, 2011). In our study, only ~38% of the respondents were employed full-time/part-time. Two items from social relationships domain also had mean below average. The participants were not that satisfied with their personal relationships (item 20; mean=2.99) and they were not satisfied with their sex life (item 21; mean=2.70). This is also not alarming as

autistic individuals struggle with their social skills and personal relationships (Orsmond, Krauss, & Seltzer, 2004). Not surprisingly, for item 26 (mean=2.92) belonging to the psychological domain, participants reported that they "seldom" to "most often" had negative feelings such as blue mood, despair, anxiety and depression. Multiple studies have shown depression and anxiety as common psychiatric comorbidities among adults with autism (Gillott & Standen, 2007; Joshi et al., 2013). Missing data for WHOQOL-BREF in this study was minimal in this study, suggesting ease of understanding of the instrument among adults with autism.

Construct validity

As depicted in other studies, we also found significant correlation between the four domains (physical, psychological, social and environment) in this study (Hanestad, et al., 2004; Skevington, et al., 2004; Yao, et al., 2002). The highest correlation was found between environment and physical domains. We also found significant correlation between four domains with overall QOL and general health items supporting construct validity. This suggests that all the domains positively contributed towards general health and overall QOL among adults with autism. Physical health was the best predictor of general health, followed by psychological heath. Environment, physical, and social health had significant positive influence on overall QOL. The percentage of variance explained by all four WHOQOL-BREF domains was 44% for overall QOL and 42% for general health.

We found good support for convergent and discriminant validity of WHOQOL-BREF in our study. Based on the corrected item-total correlation and item-to-other scale correlation values, we found higher correlation between items and their theoretically related domains and lower correlation with other theoretically un-related domains in this study for vast majority of items. Two items did have higher correlation with other domains. Item 15 related to mobility

("how well are you able to get around?" which is part of physical domain) had a higher correlation with environment domain. This may reflect an overlap in the underlying content of these two items. Nevertheless, both items still had more than acceptable correlation coefficient (r>0.04) with their own domains. Therefore, our data provides support for convergent and discriminant validity among adults with autism.

Factorial validity of WHOQOL-BREF instrument was tested by comparing one-factor model and four-factor hierarchical model. Studies in the past have conceptualized WHOQOL-BREF as a second-order model where the second-order QOL (a latent variable) had direct effects on first-order factors (measured variables) such as physical health, psychological health, social relationships and environment domains (Masthoff, et al., 2005; Miller, et al., 2008; Skevington, et al., 2004; Xia, et al., 2012; Yao, et al., 2002). We found similar results where second-order model was found to have a better fit for adults with autism. Minor modifications driven by data were made where error covariance were added between a few items to improve the model fit based on modification indices. For example, error covariance between items 3 (physical pain prevents daily activities) and 4 (need treatment to enjoy daily life) was correlated. It is likely that people experiencing physical pain and discomfort which is preventing them from doing routine activities will seek some kind of treatment to enjoy their everyday life. Similar to the findings in the general population, final four-factor model (with error covariance) of WHOQOL-BREF instrument was supported in the population of adults with autism. This further proves the generic use of this instrument and acceptable factorial validity among adults with autism.

Known-groups validity

The result of this study does not demonstrate full support for known-groups validity of WHOQOL-BREF instrument for adults with autisms. Significant differences between high and

low autism severity groups for physical and psychological health domains were observed; however, no significant difference for scores on social relationships and environment domains were found. While considering only the mean scores for social relationships and environment domains, expected direction was found where the domain scores were higher for low severity group with respect to high severity group. A few studies in the past comparing healthy and unhealthy groups have found weaker (Skevington, et al., 2004) or no discriminative power for environmental domain (Jang, et al., 2004; Jaracz, et al., 2006; Xia, et al., 2012; Yao, et al., 2002). The situational nature of environment domain, and its general lack of relation with an individual's health may explain the lack of emergence of known-groups validity for this domain of WHOQOL-BREF (Xia, et al., 2012). No statistical difference between low and high severity groups for social relationship domain was observed. Researchers who are planning to use the WHOQOL-BREF instrument in this population may consider the inclusion of additional items specific to adults with autism to increase the discriminating ability of social relationships domain.

Internal consistency

Internal consistency was measured using Cronbach's alpha in this study. We found excellent support for the reliability in this study with alpha coefficient of 0.91 for all items, and Cronbach's alpha above 0.70 across all domains. Unlike other studies (Hanestad, et al., 2004; Jaracz, et al., 2006; Masthoff, et al., 2005; Nedjat, et al., 2008; Skevington, et al., 2004; W. J. Taylor, et al., 2004; Trompenaars, et al., 2005; Yao, et al., 2002), we also found acceptable internal consistency support for social relationships domain (α=0.72) among adults with autism in the US.

Floor and ceiling effect

Floor and ceiling effects for WHOQOL-BREF were not observed in this population with the exception of three items displaying floor effect and two items displaying ceiling effect. The highest floor effect is depicted by item 3 (pain; 29.3%) and the highest ceiling effect by item 15 (mobility; 29.3%). Overall, the items were not skewed, indicating their acceptability for future use in this population.

Study limitations

A few limitations should be considered while interpreting the results of this study. Our sample included adults with autism who answered the questionnaire with little or no help from their caregivers. This may have resulted in higher representation of adults with Asperger's syndrome or high functioning autism. Further, only those adults who were members of the IAN were invited for participation. Therefore, the results of this study cannot be generalized to all adults with autism in the US. Considering the cross-sectional research design of this study, concurrent validity, predictive validity and test-retest reliability of the WHOQOL BREF were not determined. Future studies could use a longitudinal design to merit these properties.

Conclusion

Our result demonstrates a clear support for the psychometric properties of generic WHOQOL-BREF instrument in terms of its construct validity, reliability and floor and ceiling effects. Partial support for known-groups validity of the WHOQOL BREF was found among adults with autism. Study results indicate that the WHOQOL BREF is a suitable instrument for the assessment of QOL among adults with autism. Until autism specific QOL instruments are developed, researchers and providers could use this instrument for QOL outcome assessment in this growing population.

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CHAPTER 3

QUALITY OF LIFE AMONG ADULTS WITH AUTISM SPECTRUM DISORDERS

INTRODUCTION

Autism spectrum disorders are neurodevelopmental diseases interfering with brain activity leading to limited social communication and repetitive and restrictive behavior. One in 68 children have autism in the United States (US) (MMWR, 2014). Though estimates of autism prevalence among adults in the US are lacking, in a study conducted in the United Kingdom (UK), the prevalence of autism among adults was reported to be ~1% (Brugha et al., 2011). Autism is more prevalent among males compared to females (MMWR, 2014).

Assessing patients' quality of life (QOL) is gaining more recognition and is considered to be a clinically meaningful outcome for providers and researchers across several disease conditions including autism. With increase in life expectancy, researchers and clinicians are focusing on nonclinical factors such as QOL along with clinical factors to improve health and wellbeing of an individual. QOL is a multidimensional construct, which includes the physical, psychological, social, and environmental health of an individual. It assesses an individual's perception of their position in life, and the role of health and non-health-related factors in influencing those perceptions (WHOQOL, 1997). A few studies have found adults with autism to have poor physical and psychological health as compared to healthy peers or those with other disorders (Billstedt, Gillberg, & Gillberg, 2011; Eaves & Ho, 2008; Jennes-Coussens, Magill-Evans, & Koning, 2006; Kamio, Inada, & Koyama, 2013; Kamp-Becker, Schroder, Remschmidt, & Bachmann, 2010; Khanna, Jariwala-Parikh, West-Strum, & Mahabaleshwarkar, 2014). For example, Kamp-Becker et al. (2010) found lower QOL among adults with autism as compared to

adults with diabetes; however, the authors did report these adults to have better QOL as compared to adults with schizophrenia. In the only such study conducted among adults with autism in the US, Khanna et al. (2014) found lower physical and mental health-related quality of life (HRQOL) among adults with autism than the general population. The study found social support and coping to have a direct influence on HRQOL. It should be noted that Khanna et al. (2014) studied HRQOL and not QOL, which is a more broader construct. To date, no study has assessed QOL among adults with autism in the US.

Using a theoretical framework can enable one to better understand QOL and its underlying predictors. Wilson and Cleary's (1995) QOL model is the most commonly cited and extensively used conceptual model for QOL. The model was developed with the intention of integrating clinical variables with social science paradigm. There are five key dimensions of health outcomes in this model which are linked by causal pathways (Ferrans, Zerwic, Wilbur, & Larson, 2005; Wilson & Cleary, 1995): (1) biological and physiological factors, (2) symptom status ("physical, emotional, and cognitive symptoms perceived by a patient"), (3) functional status ("physical, psychological, social, and role function"), (4) general health perception ("patient's subjective rating of their health"), and (5) overall QOL ("how happy or satisfied someone is with life as a whole"). In addition, individual and environmental factors are included as mediating variables (see Figure 3.1). Wilson and Cleary's QOL model has been widely applied in its original or modified form in several different disease population, including HIV, cancer, opioid-dependent patients, kidney transplant patients, solid organ transplant patients, childhood cancer survivors and others (Devine et al., 2011; Ferrans, et al., 2005; Heslin et al., 2011; Maurice-Stam, Oort, Last, & Grootenhuis, 2009; Nokes et al., 2011; Schulz et al., 2012; Wettergren, Bjorkholm, Axdorph, & Langius-Eklof, 2004). For example, Maurice-Stam et al.

(2005) utilized Wilson and Cleary's QOL model along with Lazarus and Folkman's model (1984) as a guiding framework to propose a new model where background characteristics and personal and psychosocial factors (such as course of life, coping, social support, family functioning and communication about the disease) influence QOL among young adult survivors of childhood cancer.

For the purpose of this study, Wilson and Cleary's theoretical model was used as a guiding framework to study QOL among adults with autism. The modified model excluded biological and physiological variables from the original model because they are difficult to measure using survey-based research. Consistent with the original Wilson and Cleary's QOL model, a direct and an indirect path between autism severity and QOL was included in the modified model used in this study. As in the original model, a direct path between coping (adaptive and maladaptive coping), functional independence, and social support and QOL was included in the modified model used in this study (see Figure 3.1).

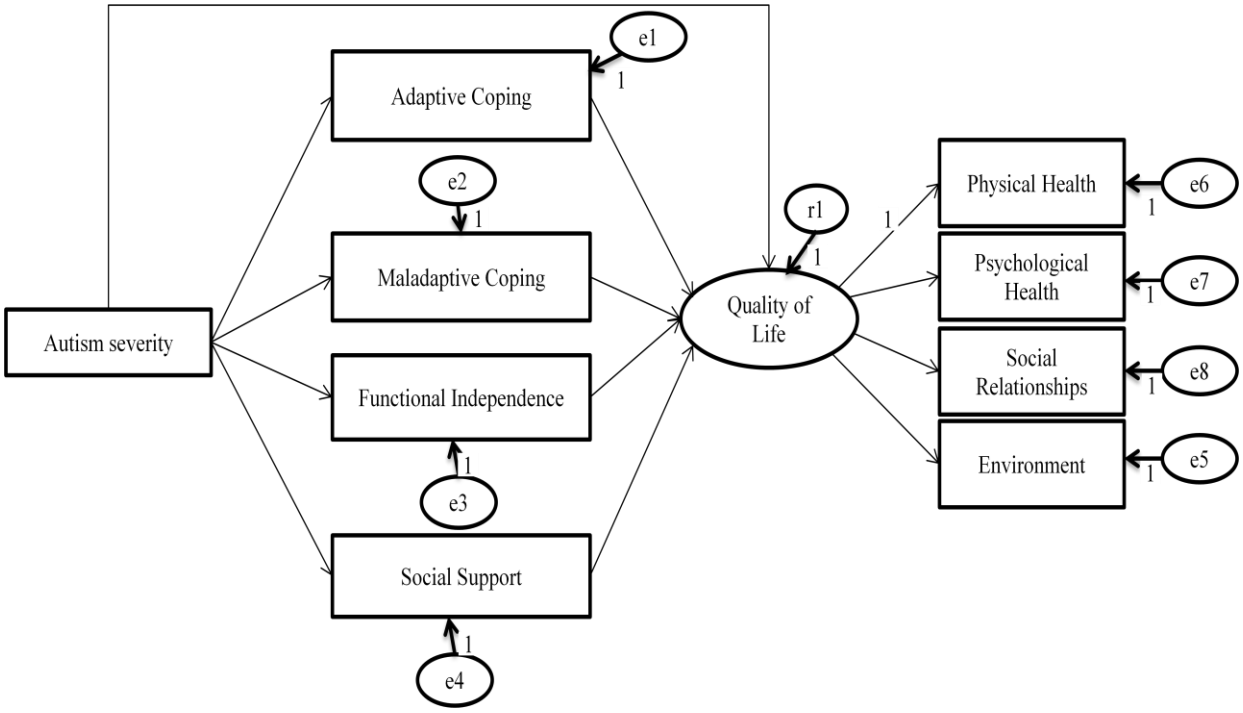

Figure 3.1: Proposed study model based on modified Wilson and Cleary's (1995) model

The relationship between QOL and autism severity has not been clearly established in the literature; however, a few studies have found autism severity to have an influence on outcomes among adults with autism (Howlin, Goode, Hutton, & Rutter, 2004; Kamio, et al., 2013; Khanna, et al., 2014). In lieu of past research in autism and previous studies of Wilson and Cleary's model, it was expected that autism severity would influence QOL among adults with the disorder. This relationship was also considered to be mediated by coping, functional independence, and social support. Coping is a process where individuals constantly make cognitive and behavioral efforts to manage internal and external demands (Folkman, Lazarus, Dunkel-Schetter, DeLongis, & Gruen, 1986). There are two types of coping mechanisms: problem-focused coping and emotional-focused coping (Folkman, et al., 1986). Problem-focused coping is viewed as adaptive coping which focuses on a disease and changing the situation to relieve the perceived problem. In contrast, emotional-focused (maladptive) coping, also considered active or avoidant coping, diverts the attention from the disease and focuses on changing the emotions and environment causing the stressful event (Abbott, Hart, Morton, Gee, & Conway, 2008; Lazarus & Folkman, 1984). Though coping is not included in the original Wilson and Cleary's model, several studies across different diseases have found it to influence QOL (Bucks et al., 2011; Burgess & Gutstein, 2007; Green, Pakenham, Headley, & Gardiner, 2002; Kaltsouda et al., 2011; Lua, Neni, & Samira, 2012; Maurice-Stam, et al., 2009; Ulvik, Nygard, Hanestad, Wentzel-Larsen, & Wahl, 2008). When the situation seems manageable, it is likely that an individual may adopt problem-focused coping strategies. However, when the situation is not amenable, then it is likely that an individual will adopt emotional-focused coping strategies (Tuncay, Musabak, Gok, & Kutlu, 2008). Adults with autism may face difficulty in coping with the disorder, especially during their transition from childhood to adulthood, due to

change in their daily life activities (McConachie, Hoole, & Le Couteur, 2011). Khanna et al. (2014) found negative association between maladaptive coping and HRQOL among adults with autism.

Functional independence is an important component that may influence QOL among adults with autism. Compared to adults with Down syndrome, adults with autism have more difficulties carrying out normal daily activities, have higher behavioral problems and receive fewer services (Esbensen, Bishop, Seltzer, Greenberg, & Taylor, 2010). Functional independence and its implications are more concerning once an individual with autism transitions from childhood to adulthood.

Social support has been reported as a key predictor of QOL among adults with autism (Burgess & Gutstein, 2007; Kamio, et al., 2013; Renty & Roeyers, 2006; Seltzer, Shattuck, Abbeduto, & Greenberg, 2004). Social support received from family and friends can lead to better outcomes among adults with autism (Seltzer, et al., 2004). Kamio et al. (2013) found a significant relationship between mothers' support and better QOL among adults with autism. Burgress and Gutsein (2007) recommended including both subjective and objective measures of social support as predictors of QOL among adults with autism. Subjective social support indicates the presence of the social network, while objective social support indicates the actual use of the available social network. Adults with autism require greater social support and services, particularly during transition from childhood to adulthood (Hendricks & Wehman, 2009). Studies have reported no peer relationship among adults with autism irrespective of their intellectual level (Howlin, et al., 2004; Orsmond, Krauss, & Seltzer, 2004). In this study, the role of social support and its relationship with QOL among adults with autism will be examined.

Several hypotheses will be tested in this study. First, it is hypothesized that greater autism severity among adults with autism will be associated with lower QOL. Second, adults with autism with better adaptive coping will have better QOL. Third, maladaptive coping will have an adverse effect on QOL. Fourth, adults with autism who have lower functional independence will experience lower QOL. Last, greater use of perceived social support among adults with autism will result in a better QOL.

RESEARCH DESIGN AND METHODS

Study design and sample

A cross-sectional, descriptive quantitative design was utilized in this study. An Internet-based survey using Qualtrics survey software system (Qualtrics Inc., Provo, UT) was administered to adults with autism enrolled with the Interactive Autism Network (IAN). IAN is the largest national, Internet-based, voluntary research registry by Kennedy Krieger Institute and is sponsored by Autism Speaks, the Simons Foundation, and the National Institute of Health (NIH) (Hall, Huerta, McAuliffe, & Farber, 2012; IAN Website, 2014). The online IAN registry is completely valid and participants are authenticated (Daniels et al., 2012). This makes an ideal option for researchers to recruit patients at IAN. Study participants were eligible for this study if they met the following criteria: 1) diagnosis of autism, Asperger syndrome or PDD-NOS from healthcare professionals; 2) aged at least 18 years; and 3) can self-report the questionnaire with little or no proxy help. The University of Mississippi's Institutional Review Board (IRB) approved (exempt status) this study.

Sample size and data collection

The relationship among variables listed in the theoretical model were studied using structural equation modeling (SEM) (further detail on the technique is provided under the 'Analysis' section). Usually, a sample size of less than 100 is considered "small", around 100-200 is considered "medium" and greater than 200 cases is "acceptable" in SEM (Harrington, 2008;

Kline, 2010). The general rule of thumb to calculate sample size where SEM is used is 10:1 (10 observations per indicator; Kline, 2010). There are 20 free parameters in this model to be estimated (seven measurement error variances, 12 regression coefficients and one residual; see Figure 3.2). Based on the recommendation of at least 10 cases per indicator, a minimum of at least 200 participants were needed for this study.

An e-mail explaining the purpose of the study and a link to the online survey was distributed to the eligible participants. The survey consisted of two parts. Part I included four measures - WHOQOL-BREF, Brief Coping Orientation to Problem Experiences (Brief-COPE; coping instrument), interpersonal support evaluation list-12 (ISEL-12; social support instrument), Waisman Activities of Daily Living Scale (functional independence instrument) and autism-quotient 10 (autism severity instrument). Part II included sociodemographic questions about adults with autism. The survey was active for three weeks (August 29 – September 19, 2013). All data was collected anonymously, and response confidentiality was assured to participants. Further, voluntary participation was emphasized. Responses were collected until the desired sample size was achieved. As a token of appreciation, a $5 incentive was provided to the participants who completed the survey.

Measures

QOL measure

A self-administered WHOQOL-BREF instrument, an abbreviated version of WHOQOL-100, was used to assess QOL among adults with autism (Skevington, Lotfy, & O'Connell, 2004). The instrument contains 26-items (one item on the 24 facets of QOL and two items measuring overall QOL and general health facets) measured on a five-point Likert scale. The 24-facets can be

further categorized into four domains: physical health (seven items), psychological health (six items), social relationships (three items) and environment (eight items). The item scores for each domain are transformed into a scale of 0-100 for easy comparison. Higher score indicates better QOL on the corresponding domain.

Autism severity instrument

Autism Quotient-10 (AQ-10), a brief version of the 50-item AQ, was used to measure autism severity among adults in this study (Allison, Auyeung, & Baron-Cohen, 2012). The scale includes the domains of social interaction, communication, attention to detail, attention switching and imagination. Responses were measured on a four-point Likert scale where 1= "strongly agree", 2= "slightly agree", 3= "slightly disagree", and 4= "strongly disagree". A higher score indicates more severity of autistic traits.

Coping instrument

Brief-COPE is a self-reported 28-item instrument to assess patients' coping strategies in response to a situation (Carver, 1997). Responses are rated on a four-point Likert scale (1=I haven't been doing this at all to 4=I've been doing this a lot). The psychometric properties of the Brief-COPE have been thoroughly documented in literature (Carver, 1997). Brief-COPE has 14 subscales: positive reframing, planning, humor, acceptance, religion, active coping, use of emotional support, use of instrumental support, behavioral disengagement, self-distraction, venting, self-blame, denial, and substance use. The subscales are further categorized into two broad scales: emotion-based (1-8) and problem-based coping (9-14). The wordings of the items were modified for the present study in order to fit the study population. Reliability of Brief-COPE in terms of internal consistency was acceptable (α =.50–.60; Carver, 1997).

Functional independence instrument

Functional independence was assessed using the 17-item Waisman Activities of Daily Living Scale (Maenner et al., 2013). The instrument is validated among adults with development disorders including autism. It includes seventeen tasks such as making bed, household tasks, errands, home repairs, laundry, bathing, grooming, dressing, toileting, simple food prep, mixing/cooking, complete meals, set/clear tables, drink from the cup, eat from the plate, wash dishes and banking finances. The items are rated based on the ability to perform tasks and overall score is created by summing up the individual items. The task may be scored as 2=”independent or does on own”, 1=”does with help” or 0=”does not do at all” (total score range 0-34). Lower scores indicate higher dependence.

Social support instrument

Interpersonal Support Evaluation List (ISEL) is a 12-item global measure of perceived social support. It has three domains: appraisal (availability of someone to interact with about problems), tangible (instrumental support), and belonging (perceived availability of people with whom one can do activities) (Cohen & Hoberman, 1983; Cohen, Mermelstein, Kamarck, & Hoberman, 1985). It is measured on a four-point Likert scale ranging from Definitely True, Probably True, Definitely False, or Probably False (range 12-48). The ISEL has acceptable internal consistency (α=0.88-0.90) and good retest reliability for subscale ranges between 0.70-0.87 (Cohen, et al., 1985). Rogers et al., (2004) validated the ISEL scale among individuals with mental illnesses. They found adequate psychometric properties (reliability and validity) of the scale among individuals with mental illnesses. A higher score indicates greater extent of perceived social support.

Sociodemographic characteristics

Age and age when diagnosed with autism (in years) were measured using an open-ended question. Gender was categorized as males and females. Ethnicity was stratified in seven categories: White, Black/African-American, Hispanic/Latino, American Indian/Alaskan Native, Asian, Native Hawaiian/Pacific Islander and other. Insurance status was assessed as: public insurance, private including HMO and no insurance. For residential status, four options (living independently, living with a partner, living with family and living in a supported home) were provided. Occupation was measured by asking if the adults were employed/self-employed full-time, employed part-time, student, seeking work or other. Educational status was measured using six categories: less than high school, high school graduate, some college, technical school, college graduate and graduate school. Marital status was assessed if the adults had been never married, not married/living with a partner, married, divorced/separated or widowed. Current diagnosis included Asperger syndrome, classic autism, or PDD-NOS. Details on co-morbid conditions, physical or mental disorders were also collected. Participants were asked if they were (yes/no) taking prescription medications. The information on autism-related treatment (yes/no) was also collected. Finally, respondents were asked if they required any assistance to complete the questionnaire (Yes/No).

Analysis

Descriptive analyses were conducted for sociodemographic variables and other measures in the study. Mean and standard deviations are reported for continuous items, and frequency and proportions are reported for categorical items. Correlations between the study measures were studied using Pearson's correlation coefficient.

As described earlier, SEM was used to study theoretical relationships. The assumptions of multivariate normality and linearity were evaluated by checking significance in skew and kurtosis index (Harrington, 2008; Kline, 2010). The absolute value of skew greater than 3.0 and kurtosis index greater than 10.0 indicates problems with the distribution. Absolute value of kurtosis index greater than 20.0 indicates serious problems with the underlying distribution of the data. Maximum likelihood estimate requires large sample size and normally distributed indicator variables. The model's fit was determined using different fit indices such as Normed Fit Index (NFI), Non-Normed Fit Index (NNFI, also known as TLI), Incremental Fit Index (IFI), Comparative Fit Index (CFI), and root mean square error of approximation (RMSEA) (Harrington, 2008; Kline, 2010; Schreiber, Nora, Stage, Barlow, & King, 2006). Following criteria was used to assess the model's fit: RMSEA < .06, TLI > .95, CFI > .95, root mean square residual (SRMR) < .08. Akaike information criteria (AIC) goodness of fit indices was used for nested models to assess the best fitting model (Kline, 2010). A smaller value of AIC indicates a better fit. The relationship of QOL among autistic adults with other factors was studied using SEM (model depicted in Figure 3.2). QOL was used as latent variable, while autism severity, social support, emotional-focused coping, problem-focused coping, functional independence, physical health, psychological health, social relationships and environment were considered as measured variables. A significance level of $p<0.05$ was used for regression coefficients. SEM analyses were conducted in SPSS AMOS version 22.0 (IBM Corporation, Armonk, NY, US).

Hierarchical linear regression was also used to predict factors affecting QOL among adults with autism. The assumptions for linear regression were tested. Data was checked for violation of linearity, homoscedasticity, independence and normality (Hair, Black, Babin, & Anderson, 2009). Independence was confirmed using Durbin-Watson statistic test (range 2-4).

R/P (residual/predicted) plots were plotted to evaluate homoscedasticity. Normality check was performed by plotting histograms. Additionally, a diagnostic test for outliers was assessed using Mahalanobis distance. Finally, multicollinearity was examined by calculating variance inflation factor (VIF; larger than 10) and tolerance (less than 0.10) for each predictor. Four separate hierarchical regressions were run with physical health, psychological health, social relationships and environmental domain scores as dependent variables. In step one, autism severity was added. In step two, coping, functional independence and social support were added. Regression analyses were conducted using SPSS version 22.0 (IBM Corporation, Armonk, NY, US).

RESULTS

Descriptive statistics

Table 3.1 depicts descriptive statistics for demographic variables. A total of 290 responses were received. 25 responses were excluded due to missing data (≥20%). A final sample of 265 responses was included for study analysis. The mean age of the adults with autism was ~33 (±13.8) years (range: 18-72 years). Majority of the participants were male (55.7%), white (82.6%) and were living with their family (45.3%). About 60% of study participants had a diagnosis of Asperger's syndrome and were not married at the time the survey was conducted. The participants also reported having comorbid mental (48.1%) and physical (40.9%) illness other than autism. The mean score of physical health was 58.90 (±18.26), psychological health was 54.59 (±16.98), social relationships was 48.26 (±23.29), and environment domain was 58.12 (±17.96), respectively (Table 3.2).

Table 3.1: Study characteristics

Characteristic	**N**	**%**
Age (in years), means (range); ±SD	33.08 (18-72)	±13.76
Age when diagnosed with autism, means (range); ±SD	22.03 (1-68)	±16.89
Gender		
Male	147	55.7
Female	115	43.6
Ethnicity		
White	218	82.6
Other	46	17.4
Insurance status		

Public insurance	112	42.4
Private including HMO	120	45.5
No insurance	30	11.4
Residential Status		
Living independently	77	29.2
Living with a partner	55	20.8
Living with family	120	45.5
Living in a supported home (group home)	10	3.8
Occupation		
Employed/Self-employed full-time	62	23.5
Employed part-time	39	14.8
Student	54	20.5
Seeking work	39	14.8
Other[¥]	70	26.5
Education level		
Less than high school	16	6.1
High school graduate	44	16.7
Some college or technical school	103	39
College graduate or graduate school	100	37.9
Marital status		
Never Married	168	63.6
Married	53	20.1
Divorced/Separated/widowed	25	9.5
Not married, living with partner	18	6.8
Primary diagnosis		
Classic autism/autistic disorder	59	22.3
Asperger's syndrome	166	62.9
Pervasive developmental disorder not otherwise specified	35	13.3
Other physical illness (yes)	108	40.9
Other mental illness (yes)	127	48.1
Prescription medications (yes)	152	57.6
Autism-related treatment (yes)	81	30.7
Behavioral therapy (yes)	45	17
Occupational therapy (yes)	27	10.2
Recreational therapy (yes)	15	5.7
Physical therapy (yes)	17	6.4
Other therapy (yes)	34	12.9
Seek Assistance to complete the survey	43	16.3
Total	**264**	**100**
[¥]Other included disabled, unemployed, volunteer, etc		

Table 3.2: Study measure descriptive					
	N	**Mean**	**Possible range**	**Minimum**	**Maximum**
Physical health	264	58.90 (18.26)	0-100	10.71	100.00
Psychological health	264	54.59 (16.98)	0-100	0.00	95.83
Social relationships	264	48.26 (23.29)	0-100	0.00	100.00
Environment	264	58.12 (17.96)	0-100	15.63	100.00
Autism severity	259	6.61 (2.29)	1-10	1.00	10.00
Adaptive coping	262	39.03 (7.81)	16-64	16.00	60.00
Maladaptive coping	262	21.14 (5.51)	10-40	10.00	37.00
Functional independence	256	23.88 (7.07)	17-51	17.00	48.00
Social Support	264	31.66 (7.74)	16-48	12.00	48.00

Correlations between study variables

Table 3.3 shows the correlation results between study measures. Autism severity was negatively correlated with psychological health among adults with autism (r=-0.154; $p<0.01$). Adaptive coping was positively correlated with psychological health (r=0.311; $p<0.01$), social relationships (r=0.357; $p<0.01$) and environmental (r=0.152; $p<0.01$) domain, respectively. A negative relationship between maladaptive coping with all the WHOQOL-BREF domains was observed (r=-0.275 – -0.350; $p<0.01$). Participants with low functional independence had significantly lower scores for physical health (r=-0.394; $p<0.01$), physiological health (r=-0.227; $p<0.01$), social relationships (r=-0.182; $p<0.01$) and environment (r=-0.327; $p<0.01$). Higher score for social support was associated with higher scores for physical health (r=0.391; $p<0.01$), psychological health (r=0.474; $p<0.01$), social relationships (r=0.511; $p<0.01$) and environment (r=0.518; $p<0.01$).

Table 3.3: Correlations between study variables				
	QOL Domains			
	Physical health	**Psychological health**	**Social relationships**	**Environment**
Autism severity	**-0.116**	-0.154*	**-0.047**	**-0.113**
Adaptive coping	**0.115**	0.311**	0.357**	0.152*
Maladaptive coping	-.0311**	-0.348**	-0.275**	-0.350**
Functional independence	-.0394**	-0.227**	-0.182**	-0.327**
Social support	0.391**	0.474**	0.511**	0.518**
***p<0.05; **p<0.01* **Bold indicates non-significant results**				

Predictors of QOL

Structural equation modeling results

Figure 3.2 depicts the modified Wilson and Cleary's model tested in the study. Model fit indices indicated poor fit of the modified model with the data (Chi-square[df] =97.13[18], *p<0.05*; GFI =0.918; CFI =0.889; RMSEA =0.13; AIC =151.13). Based on modification indices, improvements were made to the original hypothesized study model. The non-significant paths between autism severity and adaptive coping and social support and functional independence were deleted (Figure 3.2; dotted arrows). The model fit improved marginally compared to the original model (Chi-square [df] =99.302[20], *p<0.05*; GFI =0.917; CFI =0.888; RMSEA =0.126; AIC =149.302). Two covariance were specified as free parameters (adaptive and maladaptive coping and physical and social relationships). The final model had good fit with the data (Chi-square [df] =64.386[18], *p<0.05*; GFI =0.947; CFI =0.935; RMSEA = 0.1; AIC=118.386). Chi-square difference test revealed the final model fit to be better than the previous model (χ^2 difference=34.92; df=2; p<*0.001*). The final model explained 56.3%, 63.2%, 45.2% and 58.7%

of variance in physical health, psychological health, social relationships and environmental domains, respectively.

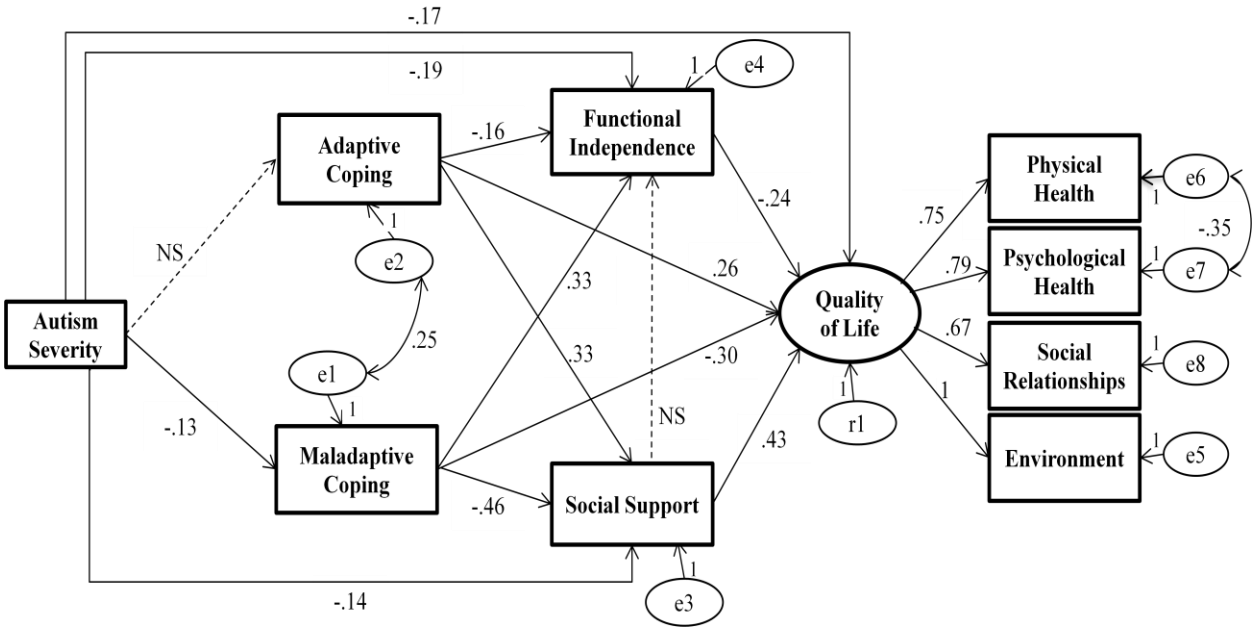

Figure 3.2: Final quality of life study model based on structural equation modeling. Goodness-of-fit indices for the above model (Chi-square = 64.39 (*P<0.001*); Chi-square/df = 3.57; GFI = 0.95; CFI = 0.94; AGFI = 0.87; RMSEA = 0.1 [90% CI 0.076, 0.129]). Dotted line represents direct non-significant relationships. Solid line represents significant relationships.

The significant direct, indirect and total effects of study variables on QOL results are presented in Table 3.4. As hypothesized, all study variables had a significant ($p<0.05$) direct effect on QOL. Autism severity had a direct negative (standardized direct effect regression weight =-0.165) as well as indirect positive effect (standardized indirect effect regression weight = 0.059) on QOL through maladaptive coping, functional independence and social support. Autism severity had a negative effect on social support (standardized direct effect regression

weight = -0.136), functional independence (standardized direct effect regression weight = -0.189) and maladaptive coping (standardized direct effect regression weight = -0.126). There was a direct significant positive relationship between social support and QOL (standardized direct effect regression weight = 0.43). We also found that the relationship between adaptive and maladaptive coping with QOL was mediated by social support. Maladaptive coping had a direct negative effect (standardized direct effect regression weight = -0.305) and adaptive coping had a direct positive effect (standardized direct effect regression weight = 0.259) on QOL. Finally, higher functional dependence was associated with better QOL (standardized direct effect regression weight = -0.237).

Table 3.4: Standardized total, direct and indirect effects

	Total effect	**Direct effect**	**Indirect effect**
Autism severity to maladaptive coping	-0.126	-0.126	
Autism severity to social support	-0.079	-0.136	0.058
Autism severity to functional independence	-0.231	-0.189	-0.042
Autism severity to quality of life	-0.106	-0.165	0.059
Adaptive coping to social support	0.329	0.329	
Adaptive coping to functional independence	-0.162	-0.162	
Adaptive coping to quality of life	0.439	0.259	0.18
Maladaptive coping to social support	-0.458	-0.458	
Maladaptive coping to functional independence	0.334	0.334	
Maladaptive coping to quality of life	-0.581	-0.305	-0.276
Functional independence to quality of life	-0.237	-0.237	
Social support to quality of life	0.43	0.43	
Only significant relationships (*p<0.05*) are shown in the table			

Hierarchical linear regression results

Table 3.5 shows the results for hierarchical linear regression to investigate the ability of autism severity, coping and social support in predicting QOL. Four separate regressions were conducted with physical health, psychological health, social relationships and environment as dependent variables of interest, respectively. There were no violations of the assumption of normality, linearity, and homoscedasticity. For all models, autism severity was added in step I, followed by adaptive coping, maladaptive coping, social support and functional independence in step II.

For physical health, autism severity was not significant in step I. After adding other mediators in step II, the total variance explained by the model as a whole was 32.8% ($p<0.001$). All the variables except adaptive coping were statistically significant. With increase in social support ($\beta = 0.64$; $p<0.001$) there was a significant increase in physical health among adults with autism, after controlling for other variables. Significant inverse relationship was observed between physical health and autism severity ($\beta = -1.34$; $p<0.05$), maladaptive coping ($\beta = -0.52$; $p<0.05$) and functional independence ($\beta = -0.87$; $p<0.001$). For psychological health, step I model was statistically significant ($\beta = -1.06$; $p<0.05$) and autism severity explained 2% of variance for psychological health. Addition of adaptive coping, maladaptive coping, social support and functional independence significantly increased the variance explained in psychological health by 36.4% ($p<0.001$). Social support and adaptive coping had a positive relationship with psychological health, with greater social support ($\beta = 0.61$; $p<0.001$) and better adaptive coping strategies ($\beta = 0.66$; $p<0.001$) leading to better psychological health. Increase in maladaptive coping strategies ($\beta = -1.02$; $p<0.001$) and autism severity ($\beta = -1.17$; $p<0.05$) were associated with lower psychological health among adults with autism. For social relationships

and environmental domains, the inclusion of autism severity in step I of the regression analyses was not statistically significant. However, the potential mediators in step II explained an additional 36.8% of variance in social relationships and 38.3% of variance in environmental domain of QOL. Increase in social support (β = 1.06; *p<0.001*) and adaptive coping strategies (β = 1.02; *p<0.001*) and decrease in maladaptive coping strategies (β = -1.04; *p<0.05*) resulted in better social relationships. For environmental domain, autism severity (β = -1.05; *p<0.05*), social support (β = 0.99; *p<0.001*), maladaptive coping (β = -0.59; *p<0.05*) and functional independence (β = -0.57; *p<0.001*) emerged as the significant predictors.

Table 3.5: Predictors of quality of life domains

	Quality of life domains			
	Physical health	**Psychological health**	**Social relationship**	**Environment**
	β (SE)	**β (SE)**	**β (SE)**	**β (SE)**
Step 1				
Autism severity	-0.81 (0.49)	-1.06* (0.46)	-0.36 (0.64)	-0.82 (0.50)
R^2	0.011	0.021	0.001	0.011
Adjusted R^2	0.007	0.017	-0.003	0.007
Step 2				
Autism severity	-1.34* (0.43)	-1.17* (0.46)	-0.14 (0.54)	-1.05* (0.41)
Adaptive coping	0.17 (0.14)	0.66** (0.12)	1.02** (0.17)	0.18 (0.13)
Maladaptive coping	-0.52* (0.21)	-1.02** (0.19)	-1.04* (0.27)	-0.59* (0.20)
Functional independence	-0.87** (0.15)	-0.22 (0.13)	-0.07 (0.18)	-0.57** (0.14)
Social support	0.64** (0.14)	0.61** (0.13)	1.06** (0.18)	0.99** (0.14)
R^2	0.328	0.381	0.369	0.390
R^2 change	0.321	0.364	0.368	0.383
Adjusted R^2	0.315	0.368	0.356	0.378

***p<0.001; *p<0.05*
***P values* were based on hierarchical linear regression**

DISCUSSION

In the present cross-sectional study, QOL among adults with autism was studied using a modified Wilson and Cleary's model. To the best of our knowledge, this is the first study to assess QOL among adults with autism in the US. Studies in the past have reported lower QOL among adults with autism; however, the factors influencing QOL have been sparsely reported. The relationship between constructs including autism severity, social support, adaptive and maladaptive coping and functional independence and QOL was examined in this study.

Results from the SEM analysis demonstrated a direct and an indirect association of autism severity with QOL. As was hypothesized, adults with severe autism were found to have lower QOL. Prior studies have reported mixed results regarding the relationship between autism severity and QOL (Kamio, et al., 2013; Kamp-Becker, et al., 2010; Renty & Roeyers, 2006). Kamio et al. (2013) found a negative relationship between aggressive behavior and social relationship domain of QOL among adults with autism in Japan. In contrast, Renty and Roeyers (2006) and Kamp-Becker et al. (2010) found no relationship between autism severity and QOL among adults with autism in Belgium and Germany, respectively. Lack of significant association in these studies may be attributable to their low sample sizes. A recent study by Khanna et al. (2014) reported a small negative correlation between autism severity and both physical and mental health domains of HRQOL in a sizable sample of adults with autism in the US. Our results indicate that autism severity may have an influence on QOL among adults with the disorder. Considering the limitations imposed by autism, it reasonable to expect variation in

QOL by severity of the disorder. With respect to individual domains of QOL instrument, we found that an increase in autism severity was associated with a decrease in physical health, psychological health and environmental QOL. As hypothesized, the relationship between autism severity and QOL was found to be mediated by modifiable variables such as maladaptive coping, functional independence and perceived social support. The impact of autism severity on QOL may alleviate if there is restricted use of maladaptive coping behaviors. Family members and clinicians could assist adults with autism in developing better coping mechanisms, which can help adults in the long-term management of symptoms and potentially improve their QOL. Alternatively, better perceived social support seems to lessen the negative impact of autism severity on QOL. Better social support from friends and family can help improve some of the symptoms such as communication skills and social engagement resulting in better QOL. Functional independence was found to attenuate the direct path between autism severity and QOL. Greater social support and the ability to perform activities of daily living may not only alleviate the impact of autism severity on QOL, but may also help these adults develop confidence in their ability to manage the symptoms associated with this disorder.

The role of coping on QOL is an understudied area among adults with autism. Only one study among adults with autism has studied the relationship between coping and HRQOL among adults with autism (Khanna, et al., 2014). The authors of the study reported a negative relationship between maladaptive coping and both physical and mental health among adults with autism. Negative relationship between maladaptive coping and all four domains of QOL was also observed in this study. Khanna et al. (2014) found no significant relationship between adaptive coping and physical and mental health in their study. We also found a direct effect of adaptive coping on QOL in our study. In their examination of coping and HRQOL, Khanna et

al. (2014) found no relationship between the two constructs. It should be noted that in regression analysis, we only found partial support for the link between adaptive coping and QOL, with adaptive coping being positively related to psychological and environmental health, but not with physical health and social relationships. Our results together with those reported by Khanna et al. (2014) reflect that adaptive coping may have an influence on psychological health and non-health related domains of QOL. Using adaptive coping to deal with a disorder like autism is less likely to bring any physical health benefits, which may explain the lack of relationship between the two constructs. Rather, positive coping techniques including positive reframing, planning, acceptance and active coping may help improve mental health of adults with the disorder. Social support and functional independence were found to mediate the relationship between adaptive and maladaptive coping and QOL in this study. Perceived social support can lead to better QOL by alleviating the effect of maladaptive coping (negative behavior) and ameliorating the effect of adaptive coping (positive behavior) among adults with autism. Together, these results highlight the critical role played by social support and coping in influencing the QOL of adults with autism.

A direct relationship between functional independence and QOL was observed in this study. An increase in functional independence was found to be associated with better physical and environmental QOL. Studies in other disease areas have reported that satisfaction with daily activities can lead to better QOL (Eklund, 2009). It has been suggested that more than a real world job, meaningful daily activities have better opportunity to improve QOL among individuals with mental illnesses. The ability to perform everyday activities satisfactorily may make individuals with mental illnesses feel more capable. As individuals with autism age, it is essential that proper training and interventions aimed at teaching them functional skills be

provided with a goal of helping them become functionally independent. This may help them better perform their day-to-day activities, which may eventually translate into an improved QOL.

Our results suggest that perceived social support plays an important role in improving QOL among adults with autism in the US. The association between perceived social support and QOL is well documented in the literature (Burgess & Gutstein, 2007; Kamio, et al., 2013; Khanna, et al., 2014; Renty & Roeyers, 2006; Seltzer, et al., 2004). Consistent with these past studies, we found perceived social support as a key positive predictor of QOL among adults with autism. Studies in the past have consistently reported unmet need in the social arena among adults with autism (Eaves & Ho, 2008; Lasgaard, Nielsen, Eriksen, & Goossens, 2010). Billstedt and researchers (2011) described the importance of suitable environment and community support among young adults with autism who are still dependent on their caretakers for activities such as education, occupation and residence. Perceived social support from siblings, friends and parents can also help in reducing loneliness among adults with autism (Lasgaard, et al., 2010). Renty and Roeyers, (2006) found perceived informal social support as a significant predictor of QOL among adults with high-functioning autism (HFA). In our study, perceived social support was found to have a positive influence on all of the individual domains of QOL (physical health, psychological health, social relationships and environment). Having social support may help adults with autism feel more acceptable and valued by their family members, friends, and the overall society.

We found the modified Wilson and Cleary's QOL conceptual model to work well in explaining the QOL of adults with autism in this study. This study represents a first step in identifying modifiable factors such as autism severity, social support, functional independence and coping as significant predictors of QOL. Unlike other studies in the past, the use of SEM

methodology allowed us to test several different relationships of key study variables (autism severity, social support, coping and functional independence) on the latent QOL variable in this study. Future research in this area could incorporate additional individual and environmental factors such as employment, role of comorbidites especially anxiety and depression levels, parental factors and others to study their influence on QOL of adults with autism. For example, anxiety and depression are the most common psychiatric co-occurring conditions among adults with autism (Boyd, Woodbury-Smith, & Szatmari, 2011; Gillott & Standen, 2007; Joshi et al., 2013; Mazzone et al., 2013). Understanding the role of such comorbid conditions and its influence on QOL may help identify additional approaches to improve overall health and QOL among adults with autism.

Limitations

A few limitations must be considered while interpreting the results of this study. The sample of this study consisted of adults with autism enrolled with IAN who had the intellectual capacity to self-report on the study questionnaire with little or no help from their caregivers. Around 63% of our study participants had a diagnosis of Asperger's syndrome, suggesting an over representation of adults with Asperger syndrome. Together these factors could restrict the generalizability of study findings. Causal relationships among study variables cannot be assumed considering the cross-sectional design used for the study. Future studies could conduct use a longitudinal design to establish more robust evidence of the predictive relationships between the variables to investigate change in perceived social support, maladaptive coping, adaptive coping, functional independence and autism severity and their association with QOL.

Conclusion

The current study builds on the literature on QOL among adults with autism. By using a well-validated theoretical framework, this study provides information on the factors interacting with QOL of adults with autism. The modified Wilson and Cleary's QOL conceptual model worked well in the study. Study results highlighted the key role played by autism severity, adaptive coping, maladaptive coping, functional independence and perceived social support in influencing QOL of adults with autism. Social support was found to have a positive influence on QOL. Further, social support was found to mediate the impact of coping on QOL. Stakeholders (caregivers, providers, and policy makers) involved in the provision of care to adults with autism must consider the role of support in improving the overall well-being of these individuals. Our results suggest that better coping strategies and more functional independence can improve QOL among adults with autism. The fact that these variables are modifiable could work as an advantage for stakeholders in improving the QOL of adults with autism. Whether it is through daily interaction with family members and friends, clinic visit with provider, or health-based interventions, there should be an effort made towards improving the QOL of adults with autism through these generally modifiable approaches.

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LIST OF APPENDICES

APPENDIX A: REVIEW OF QUALITY OF LIFE STUDIES AMONG ADULTS WITH AUTISM

Authors	Questionnaire	Proxy-reported or self-reported HRQOL	Sample and Sample size	Country
Persson, 2000	Adult and Adolescent Psycho-Educational Profile (AAPEP)	Questionnaire-Direct observation as well as staff-reported	7 adults with autism Mean age: 32.3 years (range 20-50 years)	Sweden
Jennes-Coussens et al., 2006	World Health Organization QOL-Brief (WHOQOL-BREF)	Self-administered questionnaire as well as semi-structured interview	12 adults with Asperger's syndrome Mean age: 20.3 years (range 18-21 years)	Canada
Renty and Roeyers, 2006	QOL questionnaire (QOL.Q)	Self-administered questionnaire as well as semi-structured interview	58 adults with autism Mean age: 28.34 years (range 18-53 years)	Belgium
Gerber et al., 2008	Inventaire de Qualite´ de Vie en Milieu Re´sidentiel'' (I.Q.V.M.R.)	Proxy-reported questionnaire	30 adults with autism Mean age: 39.9 years (range 24-62 years)	Switzerland
Eaves and Ho, 2008	Global rating (Overall Outcome Rating, OOR) of very good to very poor outcome	Proxy-reported (parents reported) questionnaire	48 adults with autism Mean age: 24 years (range 19-31 years)	Canada
Kamp-Becker et al., 2010	WHOQOL-BREF	Paper-based self-reported questionnaire	26 adults with autism Mean age: 21.6 years (range 17-28 years)	Germany
Billstedt et al., 2011	QOL measure I and II (QOL I and II)	Proxy-reported (staff-reported) questionnaire	108 adults with autism Mean age: 25.5 years (range 17-40 years)	Sweden
Kamio et al., 2013	WHOQOL-BREF	Paper-based self-reported questionnaire	154 adults with high functioning autism Mean age: 27.6 years (range 18-49 years)	Japan
Cottenceau et al., 2012	Vécu et Santé Perçue de l'Adolescent (VSP-A)	Paper-based self-reported questionnaire	26 adolescents with autism Mean age: 15 years (range 10-19 years)	France
Khanna et al., 2014	Short Form 12 item version 2 (SF12v2) Health Survey	Internet-based self-reported	291 adults with autism Mean age: 31 years (range 18–65years)	United States

APPENDIX B: LETTER FROM INTERACTIVE AUTISM NETWORK

February 11, 2013
Ms. Krutika Jariwala
Department of Pharmacy Administration
University of Mississippi
School of Pharmacy
238 Faser Hall
University, MS 38677

Dear Ms. Jariwala,

re: IAN (Interactive Autism Network) Project Subject Recruitment Support for
Quality of life and healthcare utilization and cost among adults with autism
(IAN Application *SR00560)*

The IAN Project would like to offer its support for the above study and your application for a 2013 Organization for Autism Research (OAR) Graduate Research Grant. The IAN Project is an innovative online project designed to accelerate the pace of autism research by linking researchers and families.

The IAN Project consists of two primary areas:

- IAN Research is an autism-focused longitudinal database and research registry designed to facilitate research efforts. Families impacted by an Autism Spectrum Disorder (ASD) share their information via the internet from the comfort of home, while researchers apply to access data or to recruit research participants. IAN Research is governed by the Johns Hopkins Medicine IRB (NA_00002750; PI Dr. Paul Law).
- IAN Community is a website and meeting place where all concerned with ASDs can gather to learn about autism research, view up-to-date IAN Research findings, and provide input into the research process.

IAN helps researchers with recruitment in two ways: by informing our participants about studies for which they qualify via email and by posting information about such studies on the IAN Community Research Opportunities Bulletin Board. To date IAN has provided recruitment and/or data services for more than 400 research studies.

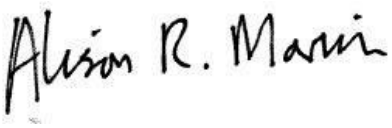
Since the launch of the project in April 2007, IAN Research has consented more 43,000 participants, including more than 15,000 children and young adults with ASD. There are currently approximately 3,000 consented individuals with ASD who are aged 18 years or older in IAN Research. Approximately, 1,000 of these have Autistic Disorder, and 2,000 have Asperger's Syndrome, PPD-NOS, or other ASD diagnosis. This represents the current participant pool for your study. Please note that over the course of your study, participants consented as children will become adults and will, thus, become eligible for the study. (We are permitted to contact the parents to let them know about your

study because they, too, are consented participants). In addition, participants will join IAN Research and may become eligible for your study.

IAN services will include: assistance with the development of the IAN subject recruitment letter for your study; selection of potentially eligible IAN participants for your study; emailing the IAN subject recruitment letter to the parents of potentially eligible IAN research participants, including a follow-up reminder email; and general assistance with IAN Subject Recruitment application. In addition, your study will be posted on the IAN Community Research Opportunities Bulletin Board, if necessary. ***For these services, IAN's estimated subject recruitment cost recovery fee will be $2,000.***

We at the IAN Project look forward to working with you on this study.

J. Kiely Law, MD, MPH
Research Director, IAN Project
Project lawk@kennedykrieger.org
443-923-4142



Alison R. Marvin, PhD
Research Coordinator/Data Manager, IAN
marvin@kennedykrieger.org
443-923-4143

APPENDIX C: COVER LETTER

IAN Subject Recruitment Sample Letter for Researcher Submission to the IRB

Dear IAN Research Participant,

When you joined the Interactive Autism Network (IAN Research Project), we promised to inform you about research projects that might be of interest to you. Below is an invitation from a team of researchers seeking IAN Research Project participants to join a new study. If you or a family member thinks that they qualify for this study and are interested in joining, please click on the study link or contact the study team directly using the information provided.

You do not have to participate in this study and your non-participation will neither affect the care you receive from any health provider nor your standing as a participant in IAN Research.

Please note that IAN Research is serving as a resource linking the autism community and researchers. This study is not endorsed by or performed under the auspices of the IAN Research project at Kennedy Krieger Institute/Johns Hopkins.

Name of Study: Quality Of Life and Healthcare Utilization and Costs among Adults with Autism Spectrum Disorder
Institution: University of Mississippi, School of Pharmacy
Location: Web-based study; no geographic limitation within the United States
Eligibility Criteria: Adults with autism spectrum disorder (ASD) or Asperger's syndrome (AS) residing in the United States who are:

- greater than or equal to 18 years of age ***and***
- able to self-report the questionnaire with little or no proxy help

Principal Investigator: Rahul Khanna, MBA, Ph.D., Assistant Professor
Contact Information: Krutika Jariwala at kjariwal@go.olemiss.edu or Dr. Khanna at 1-662-915-1651
Study Link: http://uofmississippi.qualtrics.com/SE/?SID=SV_3OEKvgYoSOj8L9b

Dear IAN Research Participant,

We would like to invite you to participate in an online research study aimed at assessing the quality of life among adults with autism. If you have already completed and submitted the survey, we thank you for your time and participation. If you have not completed the survey, we request you to kindly do so. **Survey respondents should be adults with ASD/AS who are able to complete the questionnaire independently or with minimal outside assistance**.

The online survey should take less than 10 minutes to complete. You should take this survey in one sitting to ensure that your answers are recorded. Participation in this study is voluntary and you do not have to answer questions with which you are not comfortable.

As a token of our appreciation, we will email you a $5 Amazon gift code for your participation. We will need you to provide your email address in order to send you the gift code. Your email address will not be associated with your responses, and your responses will remain confidential. You may choose not to provide your email address; however, we will not be able to send you your gift code without it. The gift code will be emailed within 2 to 4 weeks of receiving your completed response. We will send you the results of the study if we have your email address.

To join this study, click the following link:
http://uofmississippi.qualtrics.com/SE/?SID=SV_3OEKvgYoSOj8L9b
(This is the same link as the one listed in the summary information above, so you can click either one).

This study has been reviewed by The University of Mississippi's Institutional Review Board (IRB). The IRB has determined that this study fulfills the human research subject protections obligations required by state and federal law and University policies. If you have any questions, concerns, or reports regarding your rights as a participant of research, please contact the IRB at 1-662-915-7482.

We thank you in advance for your time and contribution in providing us with this valuable information. If you have questions or need more information, please do not hesitate to contact Krutika Jariwala at kjariwal@go.olemiss.edu or Dr. Khanna at 1-662-915-1651.

Warm Regards,

Dr. Rahul Khanna, M.B.A., Ph.D.
Krutika Jariwala, M.S.

Note:
IAN Research ID SR00560; the Interactive Autism Network research team can be reached at researchteam@IANproject.org

APPENDIX D: SURVEY INSTRUMENT

Survey Instrument – 1

NOTE: The survey should be completed by adults who have been diagnosed with autism spectrum disorder.

There are no right or wrong answers.

The survey has two sections:

Section I

Part I - Health and Well-Being (World Health Organization Quality of Life-Brief [WHOQOL-BREF])

Part II - Coping Strategies (Brief Coping Orientation to Problem Experiences [BRIEF-COPE])

Part III - Social Support (Interpersonal Support Evaluation List [ISEL]-12)

Part IV - Autism Severity (Autism Spectrum Quotient [AQ]-10)

Part V - Functional Independence (Activities of Daily Living [ADL])

Section II

Part I: Socio-demographics and medical history variables

Section I: Part I - Health and Well-Being

WHOQOL-BREF

Instructions:
This assessment asks how you feel about your quality of life, health, or other areas of your life. Please answer all the questions. If you are unsure about which response to give to a question, please choose the one that appears most appropriate. This can often be your first response.
Please keep in mind your standards, hopes, pleasures and concerns. We ask that you think about your life in the last two weeks. For example, thinking about the last two weeks, a question might ask:

		Very poor	Poor	Neither poor nor good	Good	Very good
1.	How would you rate your quality of life?	1	2	3	4	5

		Very dissatisfied	Dissatisfied	Neither satisfied nor dissatisfied	Satisfied	Very satisfied
2.	How satisfied are you with your health?	1	2	3	4	5

The following questions ask about how much you have experienced certain things in the last two weeks.

		Not at all	A little	A moderate amount	Very much	An extreme amount
3.	To what extent do you feel that physical pain prevents you from doing what you need to do?	5	4	3	2	1
4.	How much do you need any medical treatment to function in your daily life?	5	4	3	2	1
5.	How much do you enjoy life?	1	2	3	4	5
6.	To what extent do you feel your life to be meaningful?	1	2	3	4	5

		Not at all	A little	A moderate amount	Very much	Extremely
7.	How well are you able to concentrate?	1	2	3	4	5
8.	How safe do you feel in your daily life?	1	2	3	4	5
9.	How healthy is your physical environment?	1	2	3	4	5

The following questions ask about how completely you experience or were able to do certain things in the last two weeks.

		Not at all	A little	Moderately	Mostly	Completely
10.	Do you have enough energy for everyday life?	1	2	3	4	5
11.	Are you able to accept your bodily appearance?	1	2	3	4	5
12.	Have you enough money to meet your needs?	1	2	3	4	5
13.	How available to you is the information that you need in your day-to-day life?	1	2	3	4	5
14.	To what extent do you have the opportunity for leisure activities?	1	2	3	4	5

		Very poor	Poor	Neither poor nor good	Good	Very good
15.	How well are you able to get around?	1	2	3	4	5

The following questions ask you to say how good or satisfied you have felt about various aspects of your life over the last two weeks.

		Very dissatisfied	Dissatisfied	Neither satisfied nor dissatisfied	Satisfied	Very satisfied
16.	How satisfied are you with your sleep?	1	2	3	4	5
17.	How satisfied are you with your ability to perform your daily living activities?	1	2	3	4	5
18.	How satisfied are you with your capacity for work?	1	2	3	4	5
19.	How satisfied are you with ~~yourself?~~ your abilities?	1	2	3	4	5

20.	How satisfied are you with your personal relationships?	1	2	3	4	5
21.	How satisfied are you with your sex life?	1	2	3	4	5
22.	How satisfied are you with the support you get from your friends?	1	2	3	4	5
23.	How satisfied are you with the conditions of your living place?	1	2	3	4	5
24.	How satisfied are you with your access to health services?	1	2	3	4	5
25.	How satisfied are you with ~~your transport?~~your mode of transport?	1	2	3	4	5

The following question refers to how often you have felt or experienced certain things in the last two weeks.

		Never	Seldom	Quite often	Very often	Always
26.	How often do you have negative feelings such as blue mood, despair, anxiety, depression?	5	4	3	2	1

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Section I: Part II - Coping

INSTRUCTIONS:

These items deal with ways you've been coping with the stress in your life since you realized you have autism. Different people deal with things in different ways, but we are interested in how you've tried to deal with it. Each item says something about a particular way of coping. We want to know to what extent you've been doing what the item says. Don't answer on the basis of whether it seems to be working or not—just whether or not you're doing it. Use these response choices, please select your response for each question.

1 = I haven't been doing this at all
2 = I've been doing this a little bit
3 = I've been doing this a medium amount
4 = I've been doing this a lot

1	I've been turning to work or other activities to take my mind off things.	1	2	3	4
2	I've been concentrating my efforts on doing something about the situation I'm in.	1	2	3	4
3	I've been saying to myself "this isn't real".	1	2	3	4
4	I've been getting emotional support from others.	1	2	3	4
5	I've been giving up trying to deal with it.	1	2	3	4
6	I've been taking action to try to make the situation better.	1	2	3	4
7	I've been refusing to believe that it has happened.	1	2	3	4
8	I've been saying things to let my unpleasant feelings escape.	1	2	3	4
9	I've been getting help and advice from other people.	1	2	3	4
10	I've been trying to see it in a different light, to make it seem more positive.	1	2	3	4
11	I've been criticizing myself.	1	2	3	4
12	I've been trying to come up with a strategy about what to do.	1	2	3	4
13	I've been getting comfort and understanding from someone.	1	2	3	4
14	I've been giving up the attempt to cope.	1	2	3	4
15	I've been looking for something good in what is happening.	1	2	3	4
16	I've been making jokes about it.	1	2	3	4
17	I've been doing something to think about it less, such as going to movies, watching TV, reading, daydreaming, sleeping, or shopping.	1	2	3	4
18	I've been accepting the reality of the fact that it has happened.	1	2	3	4
19	I've been expressing my negative feelings.	1	2	3	4

20	I've been trying to find comfort in my religion or spiritual beliefs.	1	2	3	4
21	I've been trying to get advice or help from other people about what to do.	1	2	3	4
22	I've been learning to live with it.	1	2	3	4
23	I've been thinking hard about what steps to take.	1	2	3	4
24	I've been blaming myself for things that happened.	1	2	3	4
25	I've been praying or meditating.	1	2	3	4
26	I've been making fun of the situation.	1	2	3	4

Carver, C. S. (1997). You want to measure coping but your protocol's too long: Consider the Brief COPE. International Journal of Behavioral Medicine, 4, 92-100.

Section I: Part III - Social Support

INSTRUCTIONS

This scale is made up of a list of statements each of which may or may not be true about you. For each statement select "definitely true" if you are sure it is true about you and "probably true" if you think it is true but are not absolutely certain. Similarly, you should select "definitely false" if you are sure the statement is false and "probably false" if you think it is false but are not absolutely certain.

1. If I wanted to go on a trip for a day (for example, to the country or mountains), I would have a hard time finding someone to go with me.
   1. definitely false 2. probably false 3. probably true 4. definitely true

2. I feel that there is no one I can share my most private worries and fears with.
   1. definitely false 2. probably false 3. probably true 4. definitely true

3. If I were sick, I could easily find someone to help me with my daily chores.
   1. definitely false 2. probably false 3. probably true 4. definitely true

4. There is someone I can turn to for advice about handling problems with my family.
   1. definitely false 2. probably false 3. probably true 4. definitely true

5. If I decide one afternoon that I would like to go to a movie that evening, I could easily find someone to go with me.
   1. definitely false 2. probably false 3. probably true 4. definitely true

6. When I need suggestions on how to deal with a personal problem, I know someone I can turn to.
   1. definitely false 2. probably false 3. probably true 4. definitely true

7. I don't often get invited to do things with others.
   1. definitely false 2. probably false 3. probably true 4. definitely true

8. If I had to go out of town for a few weeks, it would be difficult to find someone who would look after my house or apartment (the plants, pets, garden, etc.).
   1. definitely false 2. probably false 3. probably true 4. definitely true

9. If I wanted to have lunch with someone, I could easily find someone to join me.
   1. definitely false 2. probably false 3. probably true 4. definitely true

10. If I was stranded 10 miles from home, there is someone I could call who could come and get me.
    1. definitely false 2. probably false 3. probably true 4. definitely true

11. If a family crisis arose, it would be difficult to find someone who could give me good advice about how to handle it.
    1. definitely false 2. probably false 3. probably true 4. definitely true

12. If I needed some help in moving to a new house or apartment, I would have a hard time finding someone to help me.

1. definitely false 2. probably false 3. probably true 4. definitely true

Cohen, S., Hoberman, H. M. (1983). Positive events and social supports as buffers of life change stress. Journal of Applied Social Psychology,13:99–125.

Cohen, S., Mermelstein, R., Kamarck, T., Hoberman, H. (1985). Measuring the functional components of social support. In: Sarason IG, Sarason BR, editors. Social Support: Theory, Research and Application. The Hague, Holland: Martinus Nijhoff.

Section I: Part IV- Autism Severity

Please select one option per question only:

		Definitely Agree	Slightly Agree	Slightly Disagree	Definitely Disagree
1.	I often notice small sounds when others do not.	1	2	3	4
2.	I usually concentrate more on the whole picture, rather than the small details.	1	2	3	4
3.	I find it easy to do more than one thing at once	1	2	3	4
4.	If there is an interruption, I can switch back to what I was doing very quickly.	1	2	3	4
5.	I find it easy to 'read between the lines' when someone is talking to me.	1	2	3	4
6.	I know how to tell if someone listening to me is getting bored.	1	2	3	4
7.	When I'm reading a story I find it difficult to work out the characters' intentions.	1	2	3	4
8.	I like to collect information about categories of things (e.g. types of car, types of bird, types of train, types of plant etc).	1	2	3	4
9.	I find it easy to work out what someone is thinking or feeling just by looking at their face	1	2	3	4
10.	I find it difficult to work out people's intention	1	2	3	4

Allison, C., Auyeung, B., Baron-Cohen, S. (2012) Journal of the American Academy of Child and Adolescent Psychiatry, 51(2):202-12.

Section I: Part V - Functional Independence

Instructions: "We would like to know about your current level of independence in performing activities of daily living. For each activity please select the option which best describes your ability to do the task. For example, Independent would mean you are able to do the task without any help or assistance"

PLEASE RATE YOUR'S LEVEL OF INDEPENDENCE IN...	Ability to perform task		
	2 = Independent or does on own	1 = does with help	0 = does not do at all
1. Making your own bed			
2. Doing household tasks, including picking up around the house, putting things away, light housecleaning, etc.			
3. Doing errands, including shopping in stores			
4. Doing home repairs, including simple repairs around the house, non-technical in nature; for example, changing light bulbs or repairing a loose screw			
5. Doing laundry, washing and drying			
6. Washing/bathing			
7. Grooming, brushing teeth, combing and/or brushing hair			
8. Dressing and undressing			
9. Toileting			
10. Preparing simple foods requiring no mixing or cooking, including sandwiches, cold cereal, etc.			
11. Mixing and cooking simple foods, fry eggs, make pancakes, heat food in microwave, etc.			
12. Preparing complete meal			
13. Setting and clearing table			
14. Drinking from a cup			
15. Eating from a plate			
16. Washing dishes (including using a dishwasher)			
17. Banking and managing daily finances, including keeping track of cash, checking account, paying bills, etc. (Note: if you can do a portion but not all select"does with help".)			

Maenner, M. J., Smith, L. E., Hong, J., Makuch, R., Greenberg, J., Mailick, M. R. (2013) An Evaluation of an Activities of Daily Living Scale for Adolescents and Adults with Developmental Disabilities. Disability and Health Journal, 6(1):8-17

Section II: Part I- This section collects basic socio-demographic and medical history information.

INSTRUCTIONS:

Please answer the following questions to help us better understand your responses.

1. Your age (in YEARS): _____

2. Are you: ❒ Male ❒ Female

3. What is your ethnicity? (**Please select one, only**)
   - ❒ White
   - ❒ Black/African-American
   - ❒ Hispanic/Latino
   - ❒ American Indian/Alaskan Native
   - ❒ Asian
   - ❒ Native Hawaiian/Pacific Islander
   - ❒ Other (please specify) _____

4. What kind of primary health care coverage do you have? (**Please select one, only**)
   - ❒ Medicare
   - ❒ Medicaid
   - ❒ Private including HMO
   - ❒ No insurance

5. What is your current residential status (**Please select one, only**):
   - ❒ Living independently
   - ❒ Living with a partner
   - ❒ Living with family
   - ❒ Living in a supported home (group home)

6. Which of the following describes your main occupation? **(Please select one, only)**
   - ❒ Employed/Self-employed full-time
   - ❒ Employed part-time
   - ❒ Retired
   - ❒ Student
   - ❒ Seeking work
   - ❒ Home-maker
   - ❒ Other (please specify) _____

7. What is the highest level of education that you have completed? **(Please select one, only)**
   - ❒ Less than high school
   - ❒ High school graduate
   - ❒ Some college
   - ❒ Technical school
   - ❒ College graduate
   - ❒ Graduate school

8. What is your current marital status? (**Please select one, only**)
   - ❒ Never married
   - ❒ Not married/living with a partner
   - ❒ Married
   - ❒ Divorced/separated
   - ❒ Widowed

9. Please indicate your primary diagnosis? (**Please select one, only**)
   - ❒ Classic autism/autistic disorder
   - ❒ Asperger's syndrome
   - ❒ Pervasive developmental disorder not otherwise specified (PDD-NOS)

10. Beside autism, do you have:

Other physical illness
❒ Yes (*please specify*) _____ ❒ No

Other mental (not including autism) illness
❒ Yes (*please specify*) _____ ❒ No

11. Are you currently taking any prescription medications?
❒ Yes ❒ No
If yes, please list all the prescription medications you are currently taking.
_____
_____
_____

12. Age (in YEARS) when first diagnosis with autism? _____

13. Are you currently using or have used in the past one year any autism-related treatment and program services?
❒ Yes ❒ No

If yes, please select all that applies

Behavioral therapy
❒ Yes ❒ No
Occupational therapy
❒ Yes ❒ No
Recreational therapy
❒ Yes ❒ No
Physical therapy
❒ Yes ❒ No
Other
❒ Yes, please specify _____ ❒ No

14. Did you seek assistance from anyone else (family, friend, etc.) for the purpose of completing this survey?
❒ Yes ❒ No

You will be redirected to a different server in order receive a $5 Amazon gift code. The gift code will be emailed within 2 to 4 weeks of receiving your completed response.

THANK YOU IN ADVANCE FOR YOUR TIME AND EFFORT!

Survey Instrument II:

To receive a $5 Amazon gift code, please provide your email address below:

CHAPTER 4

PREVALENCE, HEALTHCARE UTILIZATION AND COSTS, AND MEDICATION USE AMONG ADULTS WITH AUTISM ENROLLED IN THE MEDICAID PROGRAM

INTRODUCTION

Autism spectrum disorders are neurodevelopmental disorders characterized by repetitive and restrictive behavior and limited social and communication skills (American Psychiatric Association, 2000). One in 42 boys and one in 189 girls were diagnosed with autism in the United States (US) in 2014 (MMWR, 2014). The prevalence data on adults with autism in the US is not currently available; however, a study conducted in England by Bruga et al. (2011) reported that the prevalence among adults to be ~1%. Children with autism have higher healthcare utilization and expenditure in terms of outpatient visits, physician visits, medication use, emergency department encounters and inpatient hospitalizations compared to children without autism (Croen, Najjar, Ray, Lotspeich, & Bernal, 2006; Liptak, Stuart, & Auinger, 2006). In the US, the lifetime cost of supporting an adult with autism with intellectual disability (ID) is around $2.4 million while those without ID was about $1.4 million (Buescher, Cidav, Knapp, & Mandell, 2014). In addition, the mean annual cost per capita is around ~$88,000 among autistic adults with ID and ~$50,000 among those without ID. Housing, direct medical, and indirect (loss productivity) constitute the largest proportion of this cost. In general, adults with autism have been found to have higher medical cost than children with autism (Buescher, et al., 2014).

A study conducted by Nicolaidis et al. (2012) highlighted several health care disparities experienced by autistic adults in comparison with adults without autism. The authors reported that autistic adults are significantly more likely to have unmet needs in mental health, physical

health and prescription medication areas compared to non-autistic adults. The authors further reported that compared to adults without autism, adults with autism were less likely to receive preventive care services such as tetanus vaccination, blood pressure measurement and Pap smear in the last three years. In terms of healthcare utilization, the authors found that autistic adults had higher emergency room (ER) visits compared to non-autistic adults. Similar findings were reported by Iannuzzi et al. (2014) based on their analysis of the 2010 Nationwide Emergency Department Sample (NEDS) data. Adults with autism were found to have significantly higher emergency department visits compared to children with autism. In their analysis of the 2003 commercial payer MarketScan data, Shimabukaro et al. (2007) found ~4 times higher cost per year among privately insured autistic adults (18-21 years) compared to non-autistic adults. The authors further reported that adults with autism incurred ~$3,930 (~9.3 times higher) of median healthcare expenditure compared to adults without the disorder.

Studies have reported a high degree of prescription medication use (especially psychotropic drugs) among adults with autism. A recent study using longitudinal, population based cohort of adults with autism since 1980's reported that 59% of adults with autism were taking some type of psychotropic medication and about 34% had at least one psychiatric diagnosis during the study period (Buck et al., 2014). In a longitudinal evaluation (4.5 years) of medication use, Esbensen et al. (2009) reported an increase in psychotropic and non-psychotropic medication use among adolescents and adults with autism. The authors also found that out of the total sample, ~81% of adolescents and adults with autism were taking some medication and ~64% of adolescents and adults were on psychotropic medications. In addition, ~67% of their sample had at least one co-morbid condition. The authors further suggested that autistic adults and adolescents were more likely to continue their medication use once it was

initiated. Anti-psychotics and anti-depressants were the most common psychotropic drugs consumed by adolescents and adults with autism in their study. In another study, Khanna et al. (2013) utilized 2007 state Medicaid data to study the use and cost of psychotropic medication among recipients with autism. Adults with autism (≥21 years) were found to have roughly double the number of psychotropic prescription claims compared to individuals with autism aged 11-21 years (29 *vs*. 16 average drug claims per recipient).

The data on prevalence and health care utilization and cost among adults with autism enrolled in Medicaid program is not currently available. Since the Medicaid program primarily provides health coverage to low income individuals, it is essential to understand the final burden of autism in this population. The results of the study will help Medicaid state regulators to understand the economic burden of autism in adults and to provide necessary services and coverage to these individuals. The specific objectives were: 1) to estimate the trends in autism prevalence and all-cause medical services and prescription use; and 2) to study the predictors of medical services utilization and costs among adults with autism enrolled in the Medicaid program.

METHODS

Data source and study design

A retrospective descriptive analysis of 2006-2008 Medicaid administrative claims data for 39 states (Alabama, Arizona, Arkansas, California, Colorado, Connecticut, Delaware, Florida, Georgia, Idaho, Illinois, Indiana, Iowa, Kansas, Kentucky, Louisiana, Maryland, Massachusetts, Michigan, Minnesota, Mississippi, Nebraska, Nevada, New Hampshire, New Jersey, New Mexico, New York, North Carolina, Ohio, Oklahoma, Oregon, Rhode Island, South Carolina, Tennessee, Texas, Vermont, Virginia, Washington, and West Virginia) was conducted. The Medicaid Analytic Extract (MAX) data contains, 1) person summary file (demographic information and eligibility periods for the beneficiaries), 2) pharmacy claims file (medication related information), 3) other services file (outpatient hospital, physician office, and ER visits), and 4) inpatient services file (information on admission and discharge dates, diagnoses, and amount paid). The Center for Pharmaceutical Marketing and Management (CPMM) at the University of Mississippi already had the data required for this project. In order to protect privacy of the patients, information on the individual beneficiaries was encrypted with unique identification numbers where individuals are not identifiable. Study files were linked using the unique identification number. University of Mississippi Institutional Review Board (UM IRB) approval was received for the study under exempt status.

Sample selection

Recipients were eligible for the analysis if they were continuously enrolled in Medicaid throughout the study period (2006-2008) and if they were aged ≥ 18 years as of January 1, 2006 and < 65 years of age as of December 31, 2008. Recipients with long-term care claims were excluded due to the possibility of incomplete medication and hospitalization information for such individuals. Recipients with a diagnosis of autism were identified using International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) code 299.xx. A recipient with ≥1 prescription claim for a medication filled to treat autism at any time during the study year was considered as medication users. Different classes of psychotropic drugs and non-psychotropic drugs were considered based on prior literature in the area of autism (Esbensen, et al., 2009; Khanna, et al., 2013). Psychotropic drug classes included in this study were antipsychotics, antidepressants, stimulants, anxiolytics/hypnotics/sedatives and other psychotropics (antimanic drugs including lithium, valproic acid, and carbamazepine, memantine, anticonvulsants and beta blockers).

Measures

Prevalence rates

Prevalence rate among adults with autism was calculated by dividing the number of unique recipients with primary or secondary diagnosis of autism to the number of Medicaid recipients meeting the inclusion criteria per year. Rates were stratified based on demographic variables (by age, race, state, and location of residence) for each calendar year. Prevalence was reported as cases per 1,000 Medicaid recipients.

Healthcare utilization and costs

All-cause medical services costs and utilization were computed for all eligible patients for all three years (2006-2008) individually. The MAX inpatient and other therapy files were used to identify healthcare utilization and costs. The perspective of Medicaid was used to calculate cost in this study. The results were further stratified by age, race, and location of residence (rural and urban). Healthcare utilization and expenditures in terms of physician visits, ER visits, diagnostic or laboratory tests, hospitalizations (length of stay), outpatient hospital visits and prescription refills were assessed. Utilization variables, measured as counts of unique visits and expenditures, were measured by summing all the costs associated with the visits. Rates of beneficiaries using all-cause outpatient visits, inpatient visits and ER visits were reported as visits per 10,000 Medicare beneficiaries meeting the inclusion criteria and were stratified for demographic variables for each calendar year. Psychotropic drug utilization was also reported for individual drug classes for all three years separately.

Co-morbid conditions

Three measures were coded to control for co-morbid conditions: disease severity (yes/no), Charlson Co-morbidity Index (CCI) and mental health conditions. A proxy measure for disease severity was created by identifying recipients in our sample who had acute care service utilization (hospitalization or ER visit) wherein the primary diagnosis was listed as autism. Disease severity was further categorized as 'yes' or 'no' based on whether a recipient with autism had a hospitalization/ER visit with a primary diagnosis of autism or not. The co-morbidity profile of recipients was calculated by using Deyo modification of CCI (Deyo, Cherkin, & Ciol, 1992). A proxy for other mental health conditions was also created for the following conditions: schizophrenia, Attention Deficit Hyperactivity Disorder (ADHD), bipolar

disorder, depression, anxiety and mental retardation. Co-morbid measures were assessed using data for calendar year 2006.

Other demographic variables

Age was computed as of December 31st of each year (2006-2008) in order to determine eligibility for inclusion each year. Age, race/ethnicity, gender, location of residence and geographical region stratification was also used in the analysis. Age was categorized into five groups: 18-24 years, 25-35 years, 36-45 years, 46-55 years and 56-64 years. Race was categorized as white, black, and others (consisting of more than one race and unknown race). Location of residence was classified as urban and rural based on Rural Urban Commuting Area (RUCA) codes (RUCA Data, 2013).

Analysis

Means and standard deviation or frequency and percentages were used to describe the characteristics of the study recipients, as appropriate. All analyses were conducted using Statistical Analysis Software (SAS) version 9.3 (SAS Institute Inc, Cary, NC).

Trends in prevalence and medical services utilization

Logistic regression was modeled to assess trends from 2006 to 2008 in the proportion of adults with autism (prevalence) with year as a predictor variable. The proportion of recipients (N/%) using medical services (outpatient visits, inpatient visits and ER visits) stratified by demographic variable were also reported. The mean medical services utilization was also reported for each year individually.

Trends in prescription drug utilization

The number of users, average prescription (mean with standard deviation) was reported for all the individual classes for 2006, 2007 and 2008 separately. The individual classes included in this study were antipsychotics, antidepressants, stimulants, anxiolytics/hypnotics/sedatives and other psychotropics. Information on any prescriptions as well as for any psychotropic drug use was also provided for all three years.

Predictors of healthcare utilization and costs

Bivariate analysis between all-cause outpatient visits, inpatient visits, ER visits and total expenditures with study characteristics was conducted using Wilcoxon-Mann-Whitney test or Kruskal Wallis test, as appropriate. In order to determine the predictors of all-cause outpatient, inpatient and ER visits and the total all-cause cost among adults with autism, the following analyses were conducted. Generalized linear mixed model (GLMM) with an appropriate distribution and log link was modeled. For appropriate distribution (Gaussian, Poisson, Gamma, and Inverse Gaussian) for GLMM, Modified Park test was conducted. GLMM models account for the correlation at different levels. There is a clustering effect at the state level. Using ordinary regression without accounting for clustering can lead to biased standard error estimates. Therefore, a two level model with patient at the first-level and states at the second-level was modeled. All the models were computed with age, race/ethnicity, gender and location of residence as predictor variables. Fee-for-service, CCI, mental health disorders and disease severity were added as confounders. Poisson distribution with log link was found to be the most appropriate for all the models based on Modified Park test. Results were reported using incident rate ratios. Total healthcare utilization and cost was calculated by summing all the visits or cost reimbursed by Medicaid for calendar years 2007-2008. The demographic and co-morbid

variables were calculated for year 2006. The multilevel analysis was conducted by using PROC GLIMMIX procedure in SAS version 9.3 (SAS Institute Inc, Cary, NC).

RESULTS

Prevalence rates

The prevalence rates were 2.66 per 1,000 in 2006, 3.25 per 1,000 in 2007 and 3.66 per 1,000 Medicaid beneficiaries in 2008 (Table 1). Based on the logistic regression results, the prevalence of autism among adults increased significantly from 2006 to 2008 ($p<0.001$). Across all years, prevalence rates were higher among adults aged 18-25 years (5.8/1000 in 2006, 7.1/1000 in 2007 and 8.2/1000 in 2008), males (6.8/1000 in 2006, 8.2/1000 in 2007 and 9.2/1000 in 2008) and whites (3.8/1000 in 2006, 4.5/1000 in 2007 and 5.1/1000 in 2008). The prevalence rates by the location of residence (urban vs. rural) remained stable for all three years.

Table 4.1: Prevalence rates (per 1000) by demographic variables							
	2006		**2007**		**2008**		**Percent Change from 2006 *vs.* 2008**
	N (%)	**Rates /1000**	**N (%)**	**Rates /1000**	**N (%)**	**Rates /1000**	
Autism cases (Prevalence)*	19183	2.658	24160	3.245	29745	3.659	38%
Age group							
18-25 years	13188 (68.75)	5.838	16625 (68.81)	7.149	20692 (69.59)	8.198	40%
26-35 years	4212 (21.96)	2.303	5270 (51.81)	2.831	6373 (21.43)	3.089	34%
36-45 years	1110 (5.79)	0.842	1410 (5.84)	1.077	1631 (5.48)	1.167	39%
46-65 years	673 (3.51)	0.371	855 (3.54)	0.439	1049 (3.53)	0.489	32%
Gender							
Male	13997 (72.97)	6.828	17703 (73.27)	8.207	21949 (73.79)	9.222	35%
Female	5186 (27.03)	1.003	6457 (26.73)	1.221	7796 (26.21)	1.356	35%
Race							
White	10898 (56.81)	3.749	13717 (56.78)	4.546	16793 (56.46)	5.086	36%
Black or AA	4520 (23.56)	2.394	5610 (23.22)	2.91	6514 (21.9)	3.112	30%
Hispanic	1254 (6.54)	1.013	1568 (6.49)	1.224	2064 (6.94)	1.48	46%
Other	2511 (13.09)	2.118	3265 (13.53)	2.68	4374 (14.71)	3.265	54%
Location of residence†							
Urban	15799 (83.99)	2.651	19911 (83.96)	3.241	24497 (83.98)	3.654	38%
Rural	3012 (16.01)	2.608	3803 (16.04)	3.194	4674 (16.02)	3.561	37%

Rates are expressed per total Medicaid Population in that year
***Trends in prevalence is significant based on logistic regression with year as a predictor variable**
†Based on 2013 Rural Urban Commuting Area codes

Trends in medical services users and utilization

Rates per 10,000 Medicaid patients were reported for outpatient, inpatient and ER cases (Table 2). The proportion of adults with autism having outpatient, inpatient and ER room visits were higher for age group 18-25 years, males and whites. On average, there were ~37 outpatient visits in 2006, ~35 outpatient visits in 2007 and ~36 outpatient visits in 2008 (Table 3). For all three years, adults with autism had ~1 inpatient visit per year (1.21 [±1.99] in 2006, 1.28 [±2.05] in 2007 and 1.34 [±2.03] in 2008) and ~3 ER room visits (2.52 [±3.54] in 2006, 2.54 [±3.49] in 2007 and 2.60 [±3.71] in 2008) per year.

Table 4.2: Medical services user rates (per 10,000) over three year period (2006-2008)									
	Outpatient visits cases			**Inpatient visits cases**			**Emergency room visits cases**		
	2006	**2007**	**2008**	**2006**	**2007**	**2008**	**2006**	**2007**	**2008**
Total	25.84	31.40	35.35	1.73	2.1	2.27	7.17	8.92	10.22
Age group									
18-25 years	56.55	68.8	78.76	3.24	3.78	4.37	14.71	18.24	21.59
26-35 years	22.52	27.62	30.11	1.65	2.15	2.03	6.58	8.17	8.98
36-45 years	8.31	10.62	11.49	0.93	1.19	1.14	2.83	3.82	4.04
46-65 years	3.67	4.35	4.85	0.5	0.67	0.76	1.5	1.93	2.06
Gender									
Male	66.25	79.27	88.94	3.86	4.59	30.13	17.48	21.63	24.75
Female	9.82	11.88	13.17	0.88	1.09	1.09	3.08	3.73	4.21
Race									
White	36.46	43.96	49.1	2.33	2.82	2.92	10.54	12.57	14.00
Black or AA	23.53	28.44	30.43	1.52	1.83	2.22	6.37	8.34	9.49
Hispanic	9.74	11.81	14.14	0.78	0.94	0.97	2.97	3.61	4.24
Other	20.3	25.62	31.22	1.58	1.98	2.09	4.55	6.35	8.26
Location of residence[ǂ]									
Urban	25.7	31.23	35.15	1.70	2.09	2.32	7.01	8.79	10.12
Rural	25.69	31.46	35.09	1.77	1.97	1.86	7.63	9.25	10.19
Total Cases, N	18,655	23,379	28,738	1,248	1,566	1,844	5,173	6,638	8,309
Rates are expressed per total Medicaid Population in that year **[ǂ]Based on 2013 Rural Urban Commuting Area codes**									

Table 4.3: Total medical service utilization by type of service for individual years			
	2006	**2007**	**2008**
Average outpatient visits, Mean (SD)	36.86 (55.89)	34.96 (53.17)	35.98 (56.38)
Average inpatient visits, Mean (SD)	1.21 (1.99)	1.28 (2.05)	1.34 (2.03)
Average emergency room visits, Mean (SD)	2.52 (3.54)	2.54 (3.49)	2.60 (3.71)

Trends in prescription drug utilization

The total number of recipients taking any psychotropic drug as well as the average number of any psychotropic prescriptions increased slightly over the three years (Table 4; N; Mean[SD]- 14,802; 27.30 [±20.35] in 2006, 18,465; 27.51 [±20.71] in 2007 and 22,662; 27.74 [±21.11] in 2008). The total number of recipients taking antipsychotics, antidepressants, CNS stimulus, anxiolytics/sedatives/hypnotics and other psychotropics also increased from 2006 to 2008 (Table 4). Antipsychotic drugs (10,297 in 2006; 12,922 in 2007; 15,730 in 2008) had the highest number of users followed by antidepressants (7,517 in 2006; 9,344 in 2007; 11,447 in 2008) and anxiolytics/sedatives/hypnotics (2,458 in 2006; 3,184 in 2007; 3,702 in 2008) among adults with autism for all three years.

Table 4.4: Prescription drug use by individual classes for individual years			
	2006	**2007**	**2008**
Average any prescription fills, N; Mean (SD)	17,068; 41.13 (35.46)	21,449; 41.05 (36.08)	26,355; 41.69 (36.85)
Average any psychotropic fills, N; Mean (SD)	14,801; 27.30 (20.35)	18,465; 27.51 (20.71)	22,662; 27.74 (21.11)
Average antipsychotic drug fills, N; Mean (SD)	10,297; 14.07 (9.70)	12,922; 14.24 (9.95)	15,730; 14.38(10.28)
Average antidepressants drug fills, N; Mean (SD)	7,517; 10.61 (6.45)	9,344; 10.44 (6.47)	11,447; 10.48 (6.51)
Average CNS stimulus drug fills, Mean (SD)	2,039; 9.45 (6.11)	2,758; 9.62 (6.37)	3,679; 9.60 (6.20)
Average Anxiolytic/sedatives/hypnotics drug fills, Mean (SD)	2,458; 6.50 (5.56)	3,184; 6.59 (5.49)	3,702; 6.79 (5.75)
Average Other psychotropic drug fills, Mean (SD)	9,339; 15.45 (11.97)	11,576; 15.46 (12.14)	14,194; 15.64 (12.37)
CNS, Central nervous systems. **N = Total number of people taking medications**			

Predictors of healthcare utilization and cost

Bivariate analysis

Wilcoxon-Mann-Whitney test or Kruskal Wallis test analyses showed that the all-cause medical utilization (Table 5) and total cost (Table 6) varied by different demographic variables and co-morbid factors. Utilization and cost were added for calendar years 2007 and 2008. Demographic variables were calculated for year 2006. For outpatient visits, all the variables were found to be significant where adults aged 46-65 years (97.73 [±131.46]), females (76.17 [±108.90]), white (77.56 [±122.85]) and urban location (73.02 [±107.36]) had higher outpatient visits ($p<0.001$). Recipients with higher disease severity (96.32 [±112.69] *vs.* 73.03 [±107.93]; $p<0.001$) and co-morbid mental conditions (84.97 [±111.86] *vs.* 70.68 [±106.93]; $p<0.001$) had significantly higher outpatient visits. Race and disease severity were found to be significantly associated with inpatient visits ($p<0.05$). ER visits also significantly differed based on the age groups, race and disease severity ($p<0.05$). Lastly, all-cause total cost significantly differed among all the demographic variables (except gender) and co-morbid conditions ($p<0.001$). Adults who were aged 26-35 years ($133,052.01 [±$105,488.28]), had white ethnicity ($111,628.27 [±$98,714.51]), and were located in urban location ($158,870.01 [±$148,569.59]) had higher all-cause healthcare costs for calendar years 2007-08.

Table 4.5: Differences in medical service utilization by study characteristics									
	Outpatient visits			**Inpatient visits**			**Emergency room visits**		
	Mean (SD)	**Median (Range)**	***P value***	**Mean (SD)**	**Median (Range)**	***P value***	**Mean (SD)**	**Median (Range)**	***P value***
Age group			<0.001			0.819			0.0025
18-25 years	69.45 (103.48)	33 (0–731)		0.08 (0.53)	0 (0–15)		0.99 (2.77)	0 (0–87)	
26-35 years	82.53 (118.19)	37 (0–731)		0.08 (0.45)	0 (0–8)		1.05 (2.60)	0 (0–52)	
36-45 years	80.60 (108.47)	37 (0–541)		0.09 (0.51)	0 (0–7)		0.95 (2.00)	0 (0–22)	
46-65 years	97.73 (131.46)	47 (0–608)		0.08 (0.44)	0 (0–5)		1.14 (2.23)	0 (0–18)	
Gender			0.0019			0.1084			0.7109
Male	72.78 (107.84)	34 (0–731)		0.08 (0.51)	0 (0–15)		0.99 (2.61)	0 (0–87)	
Female	76.17 (108.90)	37 (0–731)		0.09 (0.51)	0 (0–12)		1.05 (2.92)	0 (0–71)	
Race			<0.001			0.0336			0.0105
White	77.56 (122.85)	29 (0–731)		0.07 (0.42)	0 (0–5)		0.89 (2.89)	0 (0–87)	
Black	66.95 (96.89)	33 (0–731)		0.09 (0.68)	0 (0–15)		0.90 (1.99)	0 (0–22)	
Other	74.80 (106.92)	37 (0–731)		0.08 (0.46)	0 (0–12)		1.08 (2.84)	0 (0–71)	
Location of residence[†]			<0.001			0.3012			0.1378
Urban	73.02 (107.36)	34 (0–731)		0.08 (0.54)	0 (0–15)		1.00 (2.76)	0 (0–87)	
Rural	71.51 (102.51)	37 (0–731)		0.07 (0.34)	0 (0–4)		1.03 (2.36)	0 (0–30)	
Unknown	123.37 (190.34)	37 (0–731)		0.06 (0.29)	0 (0–2)		0.86 (1.67)	0 (0–9)	
Insurance			<0.001			0.3751			0.2336
Managed care	79.31 (103.14)	29 (0–731)		0.08 (0.51)	0 (0–15)		1.05 (2.96)	0 (0–71)	
Fee-for service	69.42 (111.41)	44 (0–731)		0.08 (0.52)	0 (0–12)		0.97 (2.47)	0 (0–87)	
Disease severity			<0.001			<0.001			<0.001
Yes	96.32 (112.96)	52.5 (5–608)		0.55 (1.28)	0 (0–8)		3.80 (7.19)	2 (0–87)	
No	73.03 (107.93)	34 (0–731)		0.07 (0.47)	0 (0–15)		0.94 (2.43)	0 (0–71)	
Co-morbid mental conditions			<0.001			0.3012			0.1411
Yes	84.97 (111.86)	46 (0–731)		0.06 (0.35)	0 (0–5)		1.00 (2.41)	0 (0–33)	

No	70.68 (106.93)	32 (0–731)		0.09 (0.55)	0 (0–15)		1.01 (2.75)	0 (0–87)	
***P value*s were calculated based on Wilcoxon-Mann-Whitney test or Kruskal Wallis test.** **[†]Based on 2013 Rural Urban Commuting Area codes**									

Table 4.6: Differences in healthcare expenditure by study characteristics					
	N (%)	**Mean (SD)**	**Median (Range)**	**Inter-quartile range**	***P value***
Age group					<0.001
18-25 years	6,415 (70.16)	$95,035 ($89,412)	$65,572 ($74 – $763,593)	$28,021 – $134,723	
26-35 years	2,082 (22.77)	$133,052 ($105,488)	$112,090 ($158 – $659,848)	$49,931 – $194,357	
36-45 years	447 (4.89)	$130,285 ($108,547)	$110,698 ($241 – $579,157)	$47,068 – $181,914	
46-65 years	199 (2.18)	$129,365 ($112,383)	$98,341 ($2,511 – $581,251)	$34,965 – $200,559	
Gender					0.3061
Male	6,960 (76.12)	$106,104 ($96,848)	$75,701 ($74 – $763,593)	$31,268 – $155,113	
Female	2,183 (23.88)	$106,351 ($94,737)	$79,312 ($158 – $679,358)	$34,159 – $153,342	
Race					<0.001
White	1,732 (18.94)	$111,628 ($98,715)	$83,064 ($74 – $699,309)	$34,927 – $164,168	
Black	2,015 (22.04)	$92,648 ($89,529)	$63,973 ($125 – $763,593)	$26,224 – $133,315	
Other	5,396 (59.02)	$104,859 ($94,961)	$71,507.50 ($198 – $588,610)	$34,723 – $142,839	
Location of residence					<0.001
Urban	7,513 (82.17)	$158,870 ($148,570)	$118,604 ($1,355 – $659,848)	$51,780 – $203,861	
Rural	1,481 (16.20)	$107,145 ($95,337)	$77,534 ($125 – $763,593)	$33,933 – $155,833	
Unknown	149 (1.63)	$95,879 ($92,759)	$69,406 ($74 – $667,304)	$23,561 – $144,399	
Insurance					<0.001
Managed care	5,285 (57.80)	$84,606 ($81,514)	$52,838 ($74 – $699,309)	$25,187 – $123,877	
Fee-for service	3,858 (42.20)	$135,693 ($106,718)	$113,437 ($168 – $763,593)	$51,934 – $198,058	
Disease severity					<0.001
Yes	220 (2.41)	$141,989 ($120,436)	$119,689 ($2,343 – $763,593)	$51,780 – $194,127	
No	8,923 (97.59)	$105,280 ($95,511)	$75,805 ($74 – $699,309)	$31,704 – $153,993	
Co-morbid mental conditions					<0.001
Yes	1,861 (20.35)	$129,434 ($97,890)	$111,494 ($389 – $657,388)	$51,780 – $177,567	
No	7,282 (79.65)	$100,216 ($95,041)	$67,678 ($74 – $763,593)	$28,014 – $145,319	
Total	9,143 (100.00)	$106,163 ($96343)	$76,675 ($74 – $763,593)	$31,982 – $154,786	

***P value*s were calculated based on Wilcoxon-Mann-Whitney test or Kruskal Wallis test**.
[†]Based on 2013 Rural Urban Commuting Area codes

GLMM results

GLMM was modeled to study the predictors of outpatient visits (Table 7), inpatient visits (Table 8), ER visits (Table 9) and healthcare expenditure (Table 10). Based on the GLMM results, age group 18-25 years had significantly lower outpatient visits by a factor of 0.773 compared to adults aged 46-65 years (IRR = 0.773; $p<0.01$) after controlling for other variables and state-level effect. Significantly lower outpatient visits were found among whites compared to blacks (IRR = 0.909; $p=0.001$) after controlling for other variables. Adults with autism residing in urban areas had ~1.6 times higher outpatient visits compared to those in rural areas (IRR = 1.641; $p<0.001$). None of the demographic variables were found to be significant in the GLMM analyses for inpatient visits. Only race was found to be a significant predictor of ER visits; where, after controlling for all the variables, whites had lower ER visits then blacks (IRR=0.889; $p<0.04$) and others (IRR=0.848; $p=0.01$). For all-cause expenditure, all variables were found to be significant predictors among adults with autism. Adults with autism aged 18-25 years (IRR = 0.82; $p<0.001$) had lower total cost, while adults aged 26-35 years (IRR = 1.084; $p<0.001$) and 36-45 years (IRR = 1.055; $p<0.001$) had higher total cost than those aged 46-55 years. Overall, higher expenditures were found for males compared to females (IRR = 1.024; $p<0.01$), whites compared to blacks (IRR = 1.084; $p<0.01$), and adults located in urban areas compared to rural areas (IRR = 1.415; $p<0.01$).

Table 4.7: Predictors of outpatient visits				
Variables	**Coefficient (SE)**	**IRR**	**95% CI**	***P value***
Age groups in years				
18-25 *vs.* 46-65	-0.258 (0.075)	0.773	-0.404 – -0.111	0.001
26-35 *vs.* 46-65	-0.146 (0.077)	0.864	-0.296 – 0.004	0.056
36-45 *vs.* 46-65	-0.146 (0.087)	0.864	-0.317 – 0.025	0.095
Male *vs.* Female	-0.045 (0.025)	0.956	-0.094 – 0.004	0.073
Race				
White *vs.* Black	-0.095 (0.029)	0.909	-0.152 – -0.039	0.001
White *vs.* Other	0.028 (0.032)	1.028	-0.034 – 0.089	0.381
Location of residence				
Urban *vs.* Rural	0.496 (0.099)	1.641	0.302 – 0.689	<0.0001
Unknown *vs.* Rural	0.023 (0.031)	1.023	-0.039 – 0.084	0.467
Managed care *vs.* FFS	-0.164 (0.040)	0.849	-0.242 – -0.086	<0.0001
Co-morbid Mental Conditions–Y/N	0.149 (0.028)	1.161	0.094 – 0.204	<0.0001
Disease severity –Y/N	0.265 (0.070)	1.303	0.127 – 0.402	0.000
Other comorbid conditions[†]	0.163 (0.014)	1.178	0.135 – 0.192	<0.0001

IRR, incident rate ratio; FFS, fee-for-service; CI, confidence interval
***P value*s were calculated based on Generalized Linear Mixed Model (Poisson regression)**
[†]Based on 2013 Rural Urban Commuting Area codes
[†]Based on Deyo et al., 1996
Demographic variables, comorbid conditions and disease severity were calculated for year 2006.
Total healthcare utilization variables were calculated by summing all the visits in calendar years 2007-2008.

Table 4.8: Predictors of inpatient visits				
Variables	**Coefficient (SE)**	**IRR**	**95% CI**	***P value***
Age groups in years				
18-25 *vs.* 46-65	0.105 (0.379)	1.111	-0.638 – 0.848	0.782
26-35 *vs.* 46-65	0.014 (0.389)	1.014	-0.749 – 0.777	0.972
36-45 *vs.* 46-65	-0.372 (0.460)	0.689	-1.274 – 0.530	0.419
Male *vs.* Female	-0.088 (0.131)	0.916	-0.344 – 0.168	0.500
Race				
White *vs.* Black	-0.220 (0.153)	0.803	-0.519 – 0.079	0.150
White *vs.* Other	-0.060 (0.170)	0.942	-0.393 – 0.274	0.726
Location of residence				
Urban *vs.* Rural	0.020 (0.535)	1.020	-1.030 – 1.069	0.971
Unknown *vs.* Rural	0.003 (0.165)	1.003	-0.321 – 0.327	0.986
Managed care *vs.* FFS	0.078 (0.182)	1.081	-0.279 – 0.435	0.670
Co-morbid Mental Conditions–Y/N	-0.102 (0.156)	0.903	-0.409 – 0.204	0.514
Disease severity –Y/N	1.842 (0.265)	6.307	1.323 – 2.361	<0.0001
Other co-morbid conditions[†]	0.329 (0.063)	1.389	0.205 – 0.452	<0.0001

IRR, incident rate ratio; FFS, fee-for-service; CI, confidence interval
***P value*s were calculated based on Generalized Linear Mixed Model (Poisson regression)**
[‡]**Based on 2013 Rural Urban Commuting Area codes**
[†]**Based on Deyo et al., 1996**
Demographic variables, comorbid conditions and disease severity were calculated for year 2006.
Total healthcare utilization variables were calculated by summing all the visits in calendar years 2007-2008.

Table 4.9: Predictors of emergency room visits				
Variables	**Coefficient (SE)**	**IRR**	**95% CI**	***P value***
Age groups in years				
18-25 *vs.* 46-65	0.045 (0.150)	1.047	-0.249 – 0.340	0.762
26-35 *vs.* 46-65	0.072 (0.154)	1.074	-0.230 – 0.373	0.642
36-45 *vs.* 46-65	-0.042 (0.178)	0.959	-0.391 – 0.307	0.814
Male *vs.* Female	0.000 (0.052)	1.000	-0.101 – 0.101	0.999
Race				
White *vs.* Black	-0.117 (0.058)	0.889	-0.231 – -0.003	0.044
White *vs.* Other	-0.165 (0.064)	0.848	-0.291 – -0.039	0.010
Location of residence				
Urban *vs.* Rural	-0.270 (0.196)	0.763	-0.653 – 0.113	0.167
Unknown *vs.* Rural	-0.041 (0.063)	0.960	-0.164 – 0.082	0.515
Managed care *vs.* FFS	-0.002 (0.069)	0.998	-0.137 – 0.133	0.976
Co-morbid Mental Conditions–Y/N	0.046 (0.056)	1.047	-0.065 – 0.157	0.414
Disease severity –Y/N	1.274 (0.131)	3.573	1.018 – 1.529	<0.0001
Other co-morbid conditions[†]	0.291 (0.028)	1.338	0.236 – 0.347	<0.0001

IRR, incident rate ratio; FFS, fee-for-service; CI, confidence interval
***P value*s were calculated based on Generalized Linear Mixed Model (Poisson regression)**
[ǂ]Based on 2013 Rural Urban Commuting Area codes
[†]Based on Deyo et al., 1996
Demographic variables, comorbid conditions and disease severity were calculated for year 2006.
Total healthcare utilization variables were calculated by summing all the visits in calendar years 2007-2008.

Table 4.10: Predictors of total health care expenditure				
Variables	**Coefficient (SE)**	**IRR**	**95% CI**	***P value***
Age groups in years				
18-25 *vs.* 46-65	-0.198 (0.0002)	0.820	-0.199 – -0.198	<0.0001
26-35 *vs.* 46-65	0.081 (0.0002)	1.084	0.080 – 0.081	<0.0001
36-45 *vs.* 46-65	0.053 (0.0002)	1.055	0.053 – 0.054	<0.0001
Male *vs.* Female	0.024 (0.0001)	1.024	0.023 – 0.024	<0.0001
Race				
White *vs.* Black	0.081 (0.0001)	1.084	0.081 – 0.081	<0.0001
White *vs.* Other	0.182 (0.0001)	1.199	0.182 – 0.182	<0.0001
Location of residence				
Urban *vs.* Rural	0.347 (0.0003)	1.415	0.347 – 0.348	<0.0001
Unknown *vs.* Rural	0.106 (0.0001)	1.111	0.106 – 0.106	<0.0001
Managed care *vs.* FFS	-0.453 (0.0001)	0.636	-0.453 – -0.453	<0.0001
Co-morbid Mental Conditions–Y/N	0.226 (0.0001)	1.254	0.226 – 0.227	<0.0001
Disease severity –Y/N	0.267 (0.0002)	1.307	0.267 – 0.268	<0.0001
Other co-morbid conditions[†]	0.073 (0.0001)	1.076	0.073 – 0.073	<0.0001

IRR, incident rate ratio; FFS, fee-for-service
***P value*s were calculated based on Generalized Linear Mixed Model (Poisson regression)**
[†]Based on 2013 Rural Urban Commuting Area codes
[†]Based on Deyo et al., 1996
Demographic variables, comorbid conditions and disease severity were calculated for year 2006.
Total healthcare cost was calculated by summing all the costs reimbursed by Medicaid in calendar years 2007-2008

DISCUSSION

To the best of our knowledge, this is the first study to report prevalence rates, all-cause medical utilization, prescription use and all-cause expenditure among adults with autism using multi-state Medicaid claims data. A total of 19,183 adults in 2006, 24,160 adults in 2007 and 29,745 adults in 2008 had autism across 39 state Medicaid programs. The prevalence rate of autism was 2.7 per 1,000 in 2006, 3.3 per 1000 in 2007 and 3.7 per 1,000 among Medicaid beneficiaries in 2008. This is considerably lower than 1% prevalence rates among adults in England (Brugha, et al., 2011). The lower rates may be attributed to the nature of our sample and insurance system in the US. Not all adults with autism in the US will be enrolled in Medicaid program. It is likely that adults with autism have other private insurance or no insurance to cover their needed care and treatment. Since we identified adults with autism based on medical services utilization, those adults with autism enrolled in Medicaid who did not have a claim for study year would have been excluded from our calculation. A study by Shimabukuro et al. (2007) reported administrative autism prevalence of 1.2/1000 in 2003 among privately insured adults aged 18-24 years. This is lower than what we found in our sample. With the increasing prevalence of autism among children, it is expected that prevalence rates for adults will rise, which may explain the higher prevalence rates observed in our study as compared to those reported by Shimabukuro et al. (2007).

Our study results illustrate a significant increase of 38% in the prevalence rate from 2006 to 2008. Only one study so far has reported trends in prevalence among adults, where the adult

cases with autism were reported to increase by 121.4% from 2002 to 2006 in vocational rehabilitation (VR) programs in the US (Cimera & Cowan, 2009). The increasing prevalence of autism among children may explain the trends observed among adults in this study. Similar to the general demographics distribution among individuals with autism (Boyle et al., 2011; Brugha, et al., 2011; Mandell et al., 2009), we also found higher prevalence rates among white and male adults with autism. In our study, males were ~7 times more likely (prevalence rate) to have a diagnosis of autism compared to females across all age groups. In addition, we also found higher prevalence rate among younger adults aged 18-25 years compared to other age groups. Autism is more common among children than adults (Buescher, et al., 2014; Cidav, Lawer, Marcus, & Mandell, 2012). Therefore, it is possible that with more people transitioning from childhood to adulthood, we see higher prevalence rate among younger adults.

Information on health care utilization and expenditure among adults with autism is currently limited in the US. Adults with autism on average had ~36 outpatient visits, ~1 inpatient visit and ~3 ER visits during a year. From 2006 to 2008, we found an increase in outpatient visits (36.8%), ER visits (42.25%) and prescription claims (35.56%). Similar to prevalence rates, higher medical services users were young adults (18-25 years), males and whites. As autism prevalence increases, there is likely to be an increase in healthcare burden associated with this disorder. State policy makers should consider the rising medical resource use and costs of autism in making Medicaid budget allocation decisions.

In spite of higher medical services usage among young adults, outpatient visits were significantly higher among older adults after controlling for other demographic and co-morbid conditions. This could be related to gradual progression in age leading to higher office-related visits in this population. In this study, we created three proxy variables to control for co-morbid

conditions, including a proxy variable for common mental co-morbid conditions such as schizophrenia, ADHD, bipolar disorder, depression, anxiety and mental retardation in this population. However, it is also possible that older adults have other co-morbid conditions, contributing to higher outpatient visits. For example, adults with autism are more likely to have co-morbid conditions such as intellectual disability, bowels disorder, epilepsy, autoimmune disease, sleep disorder, and others (Buck, et al., 2014; Kohane et al., 2012) compared to children with autism. Therefore, general progression of age as well as occurrence of co-morbid conditions may lead to higher outpatient visits among older adults. Though prevalence rates were higher among whites, black adults had significantly higher outpatient visits and ER visits. Racial differences have been reported among children with autism with black children having a delayed diagnosis and being less likely to receive early treatment and intervention than white children (Mandell, Listerud, Levy, & Pinto-Martin, 2002; Mandell, et al., 2009). This delay in diagnosis and treatment provision early in childhood may eventually translate to higher resource use as they transition to adulthood. It is also documented that black children have difficulties in receiving quality healthcare compared to white children with autism (Magana, Parish, Rose, Timberlake, & Swaine, 2012). Adults with autism located in urban locations compared to rural locations had higher outpatient visits. Better access to support services and resources in urban locations (compared to rural locations) could have contributed to the higher visits observed among adults located in those areas.

The average all-cause expenditure among adults with autism was around $106,163 over the two-year period. The total cost was significantly higher among older adults with autism compared to the other age groups. This finding is consistent with Cidav et al. (2012), where the authors reported an increase in expenditure with age among Medicaid recipients with autism.

Males had higher expenditures compared to females. Contrary to resource utilization (outpatient visits and ER visits), higher expenditure was found among whites compared to blacks. Adults with autism in urban locations had higher average expenditure than those in rural locations. Variation in disease severity, treatment intensity, and availability of resources may explain these differences. Further research is needed to fully understand the underlying reasons contributing to cost differential among adults with autism.

Similar to the studies in the past, we also found substantial psychotropic drug use among adults with autism. Three-fourths of adults (77.2% in 2006, 76.4% in 2007 and 76.2% in 2008) with autism were taking some type of psychotropic medication to manage their symptoms. The proportion of adults using psychotropic medication found in our study is higher than previous studies in adults (~60% [Khanna et al., 2013]) as well as children (~40% [Logan et al., 2012]; 56% [Mandell et al., 2008]; ~67% [Khanna et al., 2013]) with autism enrolled in the Medicaid program. Similar to other studies, we also found that majority of the adults to have been prescribed antipsychotics or/and antidepressants (Esbensen, et al., 2009; Khanna, et al., 2013; Logan, et al., 2012). Despite their underlying side-effect profile, antipsychotics are commonly prescribed among individuals with autism. With such high usage of antipsychotics, policy makers, providers, and caregivers of adults with autism should consider if the benefit of prescribing these drugs outweigh their risks. The average prescription for any psychotropic drug was close to 28 scripts (27.3 in 2006; 27.5 in 2007 and 27.7 in 2008), which is almost similar to an average of 29 scripts reported by Khanna et al. (2013) in Mississippi Medicaid population.

Limitations

The study has a few limitations. The identification of autism cases was based on diagnostic codes (ICD-9-CM). Misclassification or coding errors during claims processing could affect

study results. We could not estimate specific autism-related costs in this study. The all-cause medical services utilization and costs reported in this study may not reflect the true healthcare burden of autism, and may have led to an overestimation of our utilization and cost numbers. Medicaid coverage varies by state, which may have affected the results of this study. However, to account for this variation, we did add second-level (random effect) of state in the multilevel modeling analysis to account for this variation. Yet other differential factors could exist that were not addressed.

Conclusions

This is the first study to evaluate the trends in prevalence, health care utilization and predictors of health care use and costs among adults with autism enrolled across several state Medicaid programs. The results of this study demonstrated significant increase in the prevalence rate among Medicaid adults with autism over the three-year study period. We also observed an increase in medical services utilization in terms of outpatient visits, ER visits and inpatient visits from 2006 to 2008. Our results also suggest significant variation in outpatient visits, ER visits and total expenditure between different demographic variables. With rising autism prevalence, state Medicaid programs need to consider the resource impact of this rising trend, and make appropriate budgetary decisions to address the needs of this growing population.

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CHAPTER 5

SUMMARY AND FUTURE RESEARCH

STUDY SUMMARY

Over the last several years, the prevalence of developmental disabilities, particularly autism has significantly increased among children (Boyle et al., 2011). Recent estimates suggest that 1 in 68 children have autism in the Unites States (US) (MMWR, 2014). With rising prevalence among children, it is likely that similar trends will be observed among adults as these children transition to adulthood. However, few studies so far have focused on health outcomes among adults with autism. By using both primary and secondary data collection techniques, this dissertation bridges the gap in the literature by providing information on quality of life (QOL), prevalence rate and healthcare utilization and costs among adults with autism.

The psychometric properties of a generic QOL measure, i.e., WHOQOL-BREF were tested in this study (Specific Aim 1). Using such an instrument in autism may provide us insights into the thoughts and perspectives of a population for which much remains unknown. However, before WHOQOL-BREF can be used routinely among adults with autism, it is essential that we assess its psychometric profile in this population. Study findings demonstrated adequate support for the convergent validity, discriminant validity, and reliability and partial support for the known-groups validity of WHOQOL-BREF among adults with autism. We failed to find any significant differences between low and high autism severity groups for social relationships and environmental domains.

This is the first study to assess QOL and its predictors among adults with autism in the US (Specific Aim 2). By using a modified Wilson and Cleary's model, the results from this

dissertation successfully provide details on individual QOL domains (physical, psychological, social relationships and environmental) and identify potential areas for improvement in adults with autism. The role of social support, functional independence, autism severity and coping and its relationship with QOL was established using structural equation modeling (SEM) and hierarchical linear regression analyses techniques. The study results suggest significant direct (negative) and indirect (positive) impact through coping, social support and functional independence on QOL. Significant negative outcomes of maladaptive coping on QOL were observed in this study. QOL was also found to be better among adults with higher functional independence in terms of performing daily household tasks and other activities. Perceived social support was found to be a significant positive predictor of QOL.

Using multi-state Medicaid data, trends in autism prevalence and healthcare utilization and cost among adults with autism was determined (Specific Aim 3). From 2006 to 2008, we found a 38 % significant increase in the prevalence rate among adults with autism where 3.6 per 1,000 Medicaid recipients had autism in 2008. Consistent with the epidemiological data among children, higher prevalence was found among males and whites. Almost 76% of recipients were taking some type of psychotropic drug in the study period. Majority of adults were taking antipsychotics and antidepressants. The results of this dissertation suggest an urgent need of developing appropriate medication use guidelines in this population. Significant demographic variation in outpatient visits, ER visits and all-cause expenditures was observed among adults with autism. Higher ER and outpatient visits were found among blacks compared to whites. All-cause total expenditure was higher among older adults, males, and whites.

The results from this dissertation imply significant health outcome burden among adults with autism. By establishing the psychometric profile of WHOQOL-BREF, this study provides

providers and health care professionals involved in management of autism among adults with the disorder a useful approach for the assessment of QOL among such individuals. By assessing the QOL and its predictors among adults with autism, this study highlights the role played by modifiable factors such as coping and social support in influencing the QOL, and the need to incorporate such measures in autism treatment management decisions. By assessing the trends in prevalence among adults with autism enrolled in Medicaid program, this study found that the issue of rising autism prevalence is not restricted to children.

DIRECTIONS FOR FUTURE RESEARCH

Different avenues can be taken to build on current research:

Study 1. Future researchers could conduct a longitudinal study to determine concurrent validity, predictive validity and test-retest reliability of the WHOQOL-BREF instrument among adults with autism. Additional items are warranted in order to capture the social relationship domain among adults with autism. Researchers who intend to use this instrument among adults with autism should revalidate the known-groups validity with additional items for the social relationship domain.

Study 2. In our study, we had an overrepresentation of adults with Asperger's syndrome. Future studies should be conducted among a broader and more representative sample. In order to demonstrate the causal relationships between the key predictor variables (autism severity, coping, functional independence and social support) and QOL, a longitudinal study should be designed. Future studies could also include other predictors of QOL.

Study 3. The current study utilized three years (2006-2008) of multi-state Medicaid data to provide information on prevalence of autism, prescription drug use and predictors of healthcare utilization and costs among adults with autism. Future studies could utilize private insurance claims data to demonstrate if the trends observed in this study hold well in other payer populations.

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WORK EXPERIENCE

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August 2008 – December 2013
Graduate Research Assistant, Department of Pharmacy Administration, University of Mississippi

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ACADEMIC CREDENTIALS

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Doctor of Philosophy (Ph.D.), Department of Pharmacy Administration, School of Pharmacy, University of Mississippi; Oxford MS
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Master of Science (M.S.), Department of Pharmacy Administration, School of Pharmacy, University of Mississippi; Oxford MS
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PUBLICATIONS

Khanna, R., Mahabaleshwarkar, R., Holmes, E. R., **Jariwala, K**. (2015). "Pharmacists' perspectives on the Patient Protection and Affordable Care Act." *Research in Social and Administrative Pharmacy*. 2015;11(1), 111-120.

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PEER-REVIEWED PRESENTATIONS AND PUBLISHED ABSTRACTS

Jariwala-Parikh K, Wasilevich B. "Medication Adherence and Associated Health Outcomes among Adults with Bipolar Disorder I"**. Podium presentation** at 14th Annual Michigan Epidemilogy Conference in Ann Arbor, MI, March 27, 2015.

Jariwala-Parikh K, Khanna R, West-Strum D, Bentley J, Banahan B, Holmes E, Barnard M. "Prevalence, Healthcare Utilization and Costs, and Medication Use among Adults with Autism

Enrolled in the Medicaid Program." **Poster presentation** at AcademyHealth in San Diego, FL, June 8-10, 2014.

Jariwala-Parikh K, Khanna R, West-Strum D, Bentley J, Banahan B, Holmes E, Barnard M. "Quality of Life among Adults with Autism Spectrum Disorders." **Poster presentation** at International Society for Pharmacoeconomics and Outcomes Research 19th Annual International Meeting, Montreal, QC, Canada, May 31-June 4, 2014. Selected for **Best Poster Finalist** award.

Jariwala-Parikh K, Khanna R, West-Strum D, Bentley J, Banahan B, Holmes E, Barnard M. "Psychometric Properties of the World Health Organization's Quality Of Life-BREF Instrument (WHOQOL-BREF) among Adults with Autism." **Poster presentation** at International Society for Pharmacoeconomics and Outcomes Research 19th Annual International Meeting, Montreal, QC, Canada, May 31-June 4, 2014. Selected for **Best Poster Finalist** award.

Khanna R, **Jariwala-Parikh K**, West-Strum D, Mahabaleshwarkar R. "Predictors of Health-Related Quality Of Life among Adults with Autism Spectrum Disorders." **Poster presentation** at International Society for Pharmacoeconomics and Outcomes Research 19th Annual International Meeting, Montreal, QC, Canada, May 31-June 4, 2014.

Khanna R, **Jariwala-Parikh K**, West-Strum D, Mahabaleshwarkar R. "Validity and Reliability of the Medical Outcomes Study Short-Form Health Survey Version 2 (SF12-V2) among Adults with Autism." **Poster presentation** at International Society for Pharmacoeconomics and Outcomes Research 19th Annual International Meeting, Montreal, QC, Canada, May 31-June 4, 2014.

Khanna R, **Jariwala K**, Bentley J. "Hospitalization Costs and Outcomes among Elderly Cancer Patients in the United States." **Podium presentation** at International Society for Pharmacoeconomics and Outcomes Research 18th Annual International Meeting, New Orleans, LA, May 18-22, 2013.

Khanna R, **Jariwala K**, Bentley J. "Health Utility Assessment Using EQ-5D among Caregivers of Children with Autism." **Poster presentation** at International Society for Pharmacoeconomics and Outcomes Research 18th Annual International Meeting, New Orleans, LA, May 18-22, 2013.

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Jariwala K, Khanna R, West-Strum D. "Psychotropic Drug Use among Autistic Individuals Enrolled in a State Medicaid Fee-For-Service Program." **Poster presentation** at Drug Information Association 2012 48th Annual Meeting Student Poster Abstracts, Philadelphia, PA, June 24-28, 2012. (Abstract citation: *Drug Information Journal* 2012;46:494-504).

Jariwala K, Khanna R. "Hospitalization Burden in Fibromyalgia: Results from the Nationwide Inpatient Sample." **Poster presentation** at the AcademyHealth in Orlando, FL, June 24-26, 2012.

Jariwala K, Holmes E. "Primary Care Physicians' Adoption of Electronic Prescribing." **Poster presentation** at the biennial Southern Pharmacy Administration Conference (SPAC) and the Western Pharmacoeconomic Conference (WPC) meeting in Austin, TX, June 22-24, 2012.

Robinson C, **Jariwala K**, Garrick J, Abdolrasulnia M, Wasko M. "Physicians' Social Media Usage Patterns as they Seek, Scan and Share Medical Knowledge Online." **Poster presentation** at Continuing Medical Education conference in Toronto, Canada, May 30-June 2, 2012.

Jariwala K, Khanna R. "Survey of Pharmacists' Awareness and Knowledge of Autism Spectrum Disorder." **Poster presentation** at American Pharmacists Association Annual Meeting, New Orleans, LA, March 9-12, 2012 (Abstract citation: *Journal of American Pharmacist Association* 2012;52(2):238).

Jariwala K, Datar M, West-Strum D, Banahan BF III, Ross LA, Bloodworth LS. "Demographic Variation and Patient Reported Outcomes at Enrollment in a Medication Therapy Management (MTM) Program in the Mississippi Delta." **Podium presentation** at the Consortium for Health Education, Economic Empowerment and Research (CHEER) conference in Memphis, TN June 20-22, 2011.

Jariwala K, Holmes E. "Factors That Physicians Find Encouraging and Discouraging About Electronic Prescribing: A Quantitative Study." **Poster presentation** at the AcademyHealth conference in Seattle, WA, June 12-14, 2011.

Jariwala K, Holmes E. "Physicians' Experience with the Electronic Prescribing System." Poster presentation at the AcademyHealth conference in Seattle, WA, June 12-14, 2011.

Jariwala K, Holmes E. "Encouraging and Discouraging Factors about Electronic Prescribing: A Quantitative Study." **Poster presentation** at the 138th APHA Annual Meeting in Denver, CO, November 6-10, 2010.

Jariwala K, Padwal T, Banahan III BF, Holmes E. "Consumers' Satisfaction with their Current Community Pharmacy and their Likelihood to Switch to a New Pharmacy." **Podium presentation** at the 2010 Southern PharmAd meeting in Memphis TN, June 18-20, 2010.

Shahpurwala Z, **Jariwala K**, Yang Y. "Cost-effectiveness of Using Saxaglitin Compared with Sitagliptin in Treating Type II Diabetes from a US Third-party Payer Perspective." **Poster presentation** at Drug Information Association 2010 46th Annual Meeting Student Poster Abstracts, Washington, DC, June 13-17, 2010. (Abstract citation: *Drug Information Journal* 2010:44; 505-511).

Jariwala K, Banahan BF III, Yang Y, Pace PF. "Adherence and Persistence among Type II Diabetic Patients Starting Monotherapy on Oral Hypoglycemic Agents." **Poster presentation** at

the International Society for Pharmacoeconomics and Outcomes Research 15th Annual International Meeting, Atlanta, GA, May 15-19, 2010.

Athavale A, **Jariwala K**, Lokhandwala T, Padwal T, Verma S, Banahan III BF, Holmes ER. "Comparing Patients' Compliance Attitudes and Behaviors with their Perceived Value for RxSync ServiceSM Components." **Poster presentation** at American Pharmacists Association Annual Meeting, Washington, DC, March 11-15, 2010.

Verma S, **Jariwala K**, Athavale AS, Lokhandwala T, Padwal T, Banahan III BF, Holmes ER. "An Assessment of Perceived Value and Willingness to Pay for RxSync Service[SM]." **Poster presentation** at American Pharmacists Association Annual Meeting, Washington, DC, March 11-15, 2010.

AWARDS, HONORS AND VOLUNTEER EXPERIENCE

2014	**Best Poster Finalist**, ISPOR 2014
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2010 – 2011	**Secretary**, International Society for Pharmacoeconomics and Outcomes Research
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2008 – 2010	**Senator**, Graduate School Council, University of Mississippi

COMPLETED COURSEWORK

Applied Longitudinal Modeling, Applied Multivariate Analysis, General Linear Models, Pharmacoepidemiology, Pharmaceutical and Healthcare Policy, Secondary Data Techniques, Pharmacoeconomics, Research Methods, Introduction to Epidemiology , Primary Data Techniques, Quantitative Methods in Psychology, Health Economics, Drug Development and Marketing, Marketing Strategy Management, Customer Relationship Management, Advanced Pharmaceutical Marketing and Patient Behavior, Advanced Studies in Consumer Behavior, Theoretical Foundations of Marketing.