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Determining Physician And Patient Characteristics That Predict The Use Of Atypical Antipsychotics In Children With Mental Health Disorders

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DETERMINING PHYSICIAN AND PATIENT CHARACTERISTICS THAT PREDICT THE USE OF ATYPICAL ANTIPSYCHOTICS IN CHILDREN WITH MENTAL HEALTH DISORDERS

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ABSRACT

Objectives: The objective of this study is to determine how patient and physician level factors influence decisions to prescribe atypical antipsychotics to children (under 18years) diagnosed with mental health disorders.

Methods: This study is a cross-sectional survey of general practitioners and psychiatrists. A web-based patient simulation survey using fractional factorial design was administered with the help of a commercial vendor. Respondents were presented with simulated patient profiles that contained various levels of factors hypothesized to be important in decision making. Physician treatment decisions were measured along with demographics and beliefs about available products. Marginal modelling using general estimating equations was used for analysis.

Results: Patient age, disease severity, physician specialty and beliefs about evidence supporting use of the drug were found to significantly influence physician prescribing decisions.

Conclusions: This study shows the factors important to decision making for physicians from different specialties and can help improve clinically appropriate and safe use of antipsychotics.

DEDICATION

This thesis is dedicated to Amma and Appa, my mom and dad, for all their support and love from over 8,000 miles away.

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Thank you!

Sujith Ramachandran

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CHAPTER I

BACKGROUND

INTRODUCTION

Atypical antipsychotics (AP) have been in the market since Clozapine was introduced in 1989 (Malone, Sheikh & Zito, 1999). They were approved by the United States Food and Drug Administration (FDA) in adults for mood disorders at the time of release and gained a lot of popularity because they possessed the effect of conventional antipsychotics while not causing severe extra pyramidal side-effects such as akasthisia, parkinsonism, dystonia and tardive dyskinesia (Pathak, West, Martin, Helm & Henderson, 2010). This factor helped spur a phenomenal increase in their use in adults, as well as in children. Since then, many other APs, such as ziprasidone, olanzapine, aripiprazole, paliperidone, have also been approved by the FDA. Their use in children had been of particular concern since there were no clinical trials supporting such use at the time (Malone, Sheikh & Zito, 1999).

The newer APs have been approved for use in diseases such as schizophrenia and bipolar disorder (Pathak et al, 2010). The use of these drugs for the treatment of conduct disorder, hyperactivity disorder, Attention Deficit Hyperactivity Disorder (ADHD), Tourette's syndrome, has not been approved yet due to the lack of evidence supporting such use. However, this unapproved use, or 'off-label use', as it is called, is well known and quite common. Despite the lack of evidence, FDA does not restrict use of drugs for unapproved indications. In fact the FDA has stated that it does not, in any way, limit the manner in which the physician chooses to use a drug (Texas Department of Family and Protective Services, 2010). A research study highlights that APs are prescribed outside their indication about 70% of the time (Farah, 2005). Staller, Wade & Baker (2005) found that 77% of APs are used in youth who do not even have a psychotic disorder. Research shows that the number of children covered by Medicaid using APs has doubled from 2001 to 2005 (Pathak et al, 2010). Use in children under 18 years has accounted for 15% of

total use of antipsychotics in 2004 - 2005. This number was as low as 7% back in 1996 – 1997 (Domino & Swartz, 2008). Further study reveals that among children, foster children use more psychotropic medications in general than non-foster children. Foster children account for only 3% of the population of Medicaid children, but they use almost 9 times as many antipsychotics as the non-foster children (Crystal, Olfson, Huang, Pincus & Gerhard, 2009).

There is limited evidence studying the effects of these drugs in children, but most existing studies point towards a range of serious adverse events such as weight gain, diabetes, hypertension, metabolic and endocrine abnormalities, hyperprolactinemia and dyslipidemia in the short term and several other unknown long-term effects (Vitiello et al., 2009; McIntyre & Jerrell, 2008; Federowicz & Fombonne, 2005; Kumra et al., 2008). With increasing budgetary constraints, payers such as Medicaid have sought to better understand the use of these drugs in children (Surles, 2005). This has made the 'off-label' prescribing of APs in children and adolescents, between the ages of 4 to 17 years, a major area of concern.

In 2011, a Government Accountability Office (GAO) study examined the rates of use of psychotropic medication among foster children in several states and recommended to the Department of Health and Human Services that they should provide guidance to states on best practices for overseeing psychiatric prescriptions (Kutz, 2011). In response to this, the Department of Health and Human Services sent a letter to the state Medicaid directors making them aware of the results of the GAO study that provides evidence towards the growing problem of safe, appropriate and effective use of psychiatric prescriptions among foster children. They proposed an expansion of activities and collaboration between the Administration for Children and Families (ACF), The Center for Medicare and Medicaid Services (CMS) and the Substance Abuse and Mental Health Services Administration (SAMHSA). This includes expansion of online resources and webinars, development of quality measures to evaluate states, working with states to enhance Drug Utilization Review, building Health Homes, encouraging use of Health Information Technology and development of guidelines for the use of psychiatric medications in children

and adolescents along with the American Academy of Child and Adolescent Psychiatry (AACAP) (DHHS, personal communication, November 23, 2011).

The increasing recognition from the FDA and the Department of Health and Human Services demonstrates the importance of addressing the issue of use of APs in children. The guidelines to be issued by SAMHSA and the AACAP dealing with appropriate use of APs in children hold the potential to revolutionize today's antipsychotics market. This study aims to help understand the process of prescription decisions better so all of the players in the health care system can plan for better ways to assure more efficient and safer use of APs in children and adolescents. The objective of the study is to find the patient and physician level factors that influence the physician's decision to prescribe APs in children and adolescents for various indications

.LITERATURE REVIEW

Physician prescription decisions

Several researchers have compared prescription decisions to an art that goes beyond mere pharmacological factors. It has been called a complex skill that requires the physician to carefully evaluate the patient's physical, psychological, social and behavioral illnesses and weigh the benefits and risks of each treatment alternative and comparing it to the option of not treating the indication (Howie, 1976).

There is also a lot of evidence to suggest that prescription decision making is not dependent only upon clinical factors. In his study on antibiotic use in cases of sore throat, Howie demonstrated that psychological, behavioral and social information about the patient can substantially influence prescription decisions (Howie, 1976). Harris (1980) goes a little further to suggest that when the decision making is in an area that is recognized as 'pharmacologically dubious', social factors influence prescribing. Bradley (1992a) made several attempts to identify the factors causing 'uncomfortable prescribing decisions' among physicians to better understand the psychological decision making process.

In an experimental study conducted in Peru to understand the factors influencing prescribing behavior in treatment of childhood diarrhea, it was found that while physicians seemed to possess adequate knowledge about conditions under which antibiotics are required in childhood diarrhea, their prescribing patterns did not appear to match their clinical beliefs. The article concluded that knowledge about disease seems to make very little difference as to what the physician prescribes. They describe the decision making process as social and not logical. The researchers further narrowed down the social

factors to a few important ones such as the physician's role as a socially defined good practitioner, previous experiences with diarrhea cases and sometimes even deficiencies in knowledge. A few other factors such as the physician's length of practice, perception of the family's expectations also seemed to influence prescribing behavior (Paredes, De La Pena, Flores-Guerra, Diaz & Trostle, 1996).

In another study similarly aimed at understanding prescribing decisions, researchers found that the physicians' perceptions of patients' expectations seemed to influence prescribing behavior the most. Other factors such as the patient's age, ethnic group and symptoms also influence prescribing behavior. The physician's perception of the patient's expectations in turn seemed to depend on the patient's symptoms, complaints, age and even on the doctor's own qualifications. The study essentially pointed out the importance of patient variables in determining what is prescribed to patients (Britten & Ukomunne, 1997).

Bradley (1992b) narrowed down the list of factors influencing the decision of whether or not to prescribe into three general categories: Patient factors, physician factors and physician concern about drugs or product factors. After several interviews conducted across North England, he concludes that "age, ethnicity, social class, education, doctor's prior knowledge of patients, doctor's feeling toward the patient, communication problems and the doctor's desire to try to preserve the doctor-patient relationship" are the important patient factors; "factors relating to doctor's role perception and expectation of themselves, uncertainty, peer influences, logistic factors and the experience of medical or therapeutic misadventures" are the important physician factors; and the doctor's concerns about drugs, or product factors as it can also be called, include the drug's "side-effects, cost, risk of dependence, necessity, antibiotic resistance, efficacy" etc., in the order of their importance.

Prescribing of atypical antipsychotics

A thorough search of the literature in the field of antipsychotics research provides insight into the use of APs. Cooper et al. (2006) studied the trends in prescribing of antipsychotic medications in children.

They examined the diagnoses that were associated with the use of APs and found that nearly 29% of the use was for ADHD and conduct disorder, which was not a labeled use of the products. Bipolar disorder accounted for 23% of use, followed by 13.8% for non-psychiatric disorders. Schizophrenia, for which APs are FDA approved for use in children, could be attributed to only 13.5% of the use. The use of these drugs for approved indications grew 2.49 times between the periods 1995-1998 and 1999-2002, while the use for the unapproved indications grew by 3.52 times. Interestingly the article also concluded that 30% of all antipsychotic prescriptions were attributable to non-psychiatrists. The fact that there was a three-fold increase in the use of APs by non-mental health providers during the study period demonstrates the importance of studying use not just among mental health providers, but also among primary care physicians.

Many researchers studying the trends and patterns of use of these APs have concluded that several different factors seem to drive use. In accordance with the prescribing decision making literature, most of these factors seem to involve social information of the patient. Olfson et al. (2006) found that males seem to be receiving more APs than females. And that Medicaid insured children also are prescribed more of these than are privately insured children. While the reasons for this differential use have not been established by research, many of these patterns have been documented by several researchers (Olfson et al., 2006; Hamann, Langer, Leucht, Busch & Kissling, 2004; DHHS, personal communication, November 23, 2011).

Research points out that the differential use among various APs that exists in the market is not completely evidence based (Pathak et al., 2010). Cullen et al. (2008) attempted to analyze evidence from various open trials comparing the second generation antipsychotics head-to-head in order to establish a reason for the differential use of the products. However, because very little comparative efficacy data exists, they concluded that the physician's choice of APs depends more on the side-effect profile of each drug. The adverse effects profile for these antipsychotics has been well studied in adults, but large clinical trials or long-term studies do not exist in children and adolescents. Evidence available from an expert

panel convened by the European Neuro-psychopharmacology to study efficacy and safety data states that children and adolescents are more vulnerable to these side-effects than adults (Vitiello et al., 2009).

The patient factors influencing prescribing of APs seem to include not just their diagnoses, age and gender but even some risk factors that can make them susceptible to the side-effects of these drugs. McIntyre and Jerrell (2008), studying the pattern of adverse events associated with the use of antipsychotics in children and adolescents in the South Carolina Medicaid database, found that not only do children treated with these drugs have the risk of acquiring diseases such as obesity, type II diabetes, dyslipidemia and orthostatic hypotension among others, but certain criteria seemed to make them more vulnerable to these adverse events than others. For example, the authors concluded, patients with substance abuse disorders are at a greater risk to cardiovascular events. They also found that adolescents over 13 years old can be more vulnerable to developing type II diabetes and that girls are more likely than boys to develop obesity, type II diabetes, orthostatic hypotension and dyslipidemia (McIntyre & Jerrell, 2008). On the contrary, a meta-analysis of randomized clinical trials, looking at the safety and tolerability of APs in children concludes that males are more susceptible to weight gain than females. They also list parental body mass index (BMI) and low initial BMI as other risk factors for weight gain (Federowicz & Fombonne, 2005). The evidence available is mostly restricted to the short-term and as yet, still inconclusive.

Study significance

Even though the evidence available as of today is inconclusive, the results of these studies suggest that the adverse events caused by APs in children are not only significant, but also differential, thereby varying in effect because of the presence or absence of several risk factors. These differential adverse event profiles and risk factors may also influence the physician's prescription choice.

The letter sent to the state directors from the Department of Health and Human Services mentions that factors such as age, gender, behavioral concerns and placement type (for foster children) can affect

likelihood of being prescribed psychotropic medications (DHHS, personal communication, November 23, 2011). A study in Germany trying to decipher medical decision making in antipsychotic drug choice concludes that younger physicians are more likely to prescribe second generation antipsychotics than older or more experienced physicians (Hamann et al., 2004).

Evidence from widely varying sources point to several different potential predictors of a physician's choice to treat children and adolescents with APs. These predictors range from patient level factors, such as age, insurance, consent from parents; to physician level factors, such as type and size of practice, specialization and the propensity to adopt new practices; and even product factors such labeling status.

This study tries to measure the effect of each of physician and patient factors on the physician's decision to prescribe APs in children and adolescents. Based on the evidence presented above, the following objectives have been proposed for the study

RESEARCH OBJECTIVES

1. To determine how patient level factors, such as age, race, sex or attitude about consent from parent/guardian influence the physician's decision to prescribe atypical antipsychotics in children.
2. To determine how physician characteristics, such as specialization, mental health patient volume or beliefs about drugs influence physician's decision to prescribe atypical antipsychotics in children.

BIBLIOGRAPHY

Bradley CP. Uncomfortable prescribing decisions: a critical incident study. BMJ. 1992a; 304:294-296.

Bradley CP. Factors which influence the decision whether or not to prescribe the dilemma facing general practitioners. Brit Gen J Pract. 1992b; 42:454-458.

Britten N, Ukoumunne O. The influence of patient's hopes of receiving a prescription on doctor's perceptions and the decision to prescribe: a questionnaire survey. BMJ. 1997; 315:1506-1510.

Cooper WO, Arbogast PG, Ding H, Hickson GB, Fuchs C, Ray WA. Trends in prescribing of antipsychotic medications for US children. Ambul Pediatr. 2006; 6:79-83.

Crystal S, Olfson M, Huang C, Pincus H, Gerhard T. Broadened use of atypical antipsychotics: Safety, effectiveness and policy challenges. Health Affair. 2009; 28(5): 770. Available at: http://content. healthaffairs.org/content/28/5/w770.full.html

Cullen KR, Kumra S, Regan J, Westerman M, Charles SC. Atypical Antipsychotics for treatment of schizophrenia spectrum disorders. Psychiatric Times. 2008; 25 (3):2.

Department of Health and Human Services, Letter to State Director. Washington DC: 20201.

Domino ME, Swartz MS. Who are the new users of antipsychotic medications? Psychiatr Serv. 2008; 59:507–514.

Fedorowicz VJ, Fombonne E. Metabolic side-effects of atypical antipsychotics in children: a literature review. J Psychopharmacol. 2005; 19(5):533-550.

Hamann J, Langer B, Leucht S, Busch R, Kissling W. Medical decision making in antipsychotic drug choice for Schizophrenia. Am J Psychiatry. 2004; 161:1301-1304. Harris CM. Personal view. BMJ. 1980; 280:57.

Howie JR. Clinical Judgment and antibiotic use in general practice. BMJ. 1976; 2:1061–1064.

Kumra S, Oberstar JV, Sikich L, Findling RL, McClellan JM, Vinogradov S, Schulz SC. Efficacy and tolerability of second-generation antipsychotics in children and adolescents with schizophrenia. Schizophrenia Bull. 2008; 34(1):60-71.

Kutz GD. Foster children: HHS guidance could help states improve oversight of psychotropic prescriptions. Washington DC: General Accounting Office Report GAO – 12- 270T.Farah A. Atypicality of atypical antipsychotics. Prim Care Companion J Clin Psychiatry. 2005;7:268-274.

Olfson M, Blanco C, Liu L, Moreno C, Laje G. National trends in the outpatient treatment of children and adolescents with antipsychotic drugs. Arch Gen Psychiatry. 2006; 63:679-685.

Malone R, Sheikh R, Zito J. Novel antipsychotic medications in the treatment of children and adolescents. Psychiatr Serv. 1999;50(2): 171-174.

McIntyre RS, Jerrell JM. Metabolic and cardiovascular adverse events associated with antipsychotic treatment in children and adolescents. Arch Pediatr Adolesc Med. 2008; 162 (10):929-935.

Paredes P, De La Pena M, Flores-Guerra E, Diaz J, Trostle J. Factors influencing physician's prescribing behavior in the treatment of childhood diarrhea: Knowledge may not be the clue. Soc. Sci. Med. 1996; 42(8):1141-1153.

Pathak P, West D, Martin BC, Helm M, Henderson C. Evidence-based use of second generation antipsychotics in a state Medicaid pediatric population, 2001 – 2005. Psychiatr Serv. 2010;61 (2): 1–7.

Staller JA, Wade MJ, Baker M. Current prescribing patterns in outpatient child and adolescent psychiatric practice in New York. J Child Adolesc psychopharmacol. 2005; 15:57-61.

Surles RC. Atypical antipsychotics: Considerations for Medicaid coverage. Am J Managed Care. 2005; 11(8):S248-S253.

Texas Department of Family and Protective Services; University of Texas at Austin College of Pharmacy. (2010, December) Psychotropic Medication Utilization Parameters for Foster Children. Retrieved from: http://www.dfps.state.tx.us/Child_Protection/Medical_Services/guide-psychotropic.asp

Vitiello B, Correll C, van Zwieten-Boot B, Zuddas A, Parellada M, Arango C. Antipsychotics in children and adolescents: Increasing use, evidence for efficacy and safety concerns. Eur.Neuropsychopharmacol. 2009.04.008.

CHAPTER II

METHODOLOGY

METHODS

Study design

A cross-sectional patient simulation survey with a fractional factorial design for patient attributes was selected as the best approach for addressing the research objectives in a manner that would be as unbiased as possible.

Sample

The study employed a cross-sectional survey of psychiatrists and primary care physicians. A national sample of physicians was used so as to minimize regional bias and to maximize generalizability of results. The sampling frame included actively practicing primary care physicians and psychiatrists. In order to obtain a sufficient number of responses from both groups of respondents, stratified quota sampling was used. Two quotas were defined for the purposes of quota sampling. The first quota, psychiatrists (PSYCHs), was comprised of psychiatrists treating children and adolescents. The second quota, Primary Care Practitioners (PCPs), included family practice, internal medicine, pediatrician and general practice physicians treating children and adolescents for mental health problems..

In order to be eligible for the study, physicians were required to be engaged in full time active practice for at least 2 years post-residency. Further, physicians in the PCP quota were required to spend at least 50% of their time in outpatient care and those in the PSYCH quota were required to spend at least 25% of their time in outpatient care. Respondents were also required to have a non-zero percent of patient population under 18 years of age, diagnosed with psychosis and currently taking APs.

Sample collection

The sample was obtained through a national physician panel maintained and verified by Reckner Healthcare. Physicians invited to participate in the study had to go through a set of screener questions to determine if they were eligible for the study and to determine which quota they were in. Respondents not classified into either of the two quotas or who did not meet the criteria of any of the screening questions were terminated from the survey and thanked for their willingness to participate. Eligible respondents who completed the survey were promised a summary of the study results as an incentive for participation. No monetary incentive was provided. Physicians were informed that the survey was being conducted for researchers at the University of Mississippi and the study had been approved by the University of Mississippi Institutional Review Board in order to stress the non-biased nature of the study. The anonymity of the survey results was also stressed.

Data was collected through an on-line survey. Reckner Healthcare provided survey programming, subject recruiting and data collection. The vendor contacted potential respondents by e-mail, collected responses and provided the researcher a de-identified data set for analysis. Follow-up mailing of summary report to respondents was conducted by the vendor.

Survey design

A patient simulation survey aims to collect data from physicians by replicating their daily work environment. This technique minimizes response bias by simulating patients that a physician would potentially see in a day-to-day practice and recording the treatment decisions made for each patient. To simulate patients accurately, all information that a physician will review before treating a patient and all treatment options have to be provided to respondents. The information has to not only be complete enough, but also presented in a manner that simulates the way information of this nature would appear in a typical patient chart.

The survey took approximately 15-20 minutes to complete. The following parts of the survey were presented to the physician as part of the research study:

1. Screener: A short set of screening questions to determine that the respondents met the criteria required in the study. The specific criteria that respondents needed to meet were described in the previous section. The screener also included some questions about physician practice characteristics. Variables measured in this section included years spent in active practice post-residency, mental health patient volume in a typical week, proportion of patient population less than or equal to 18 years of age, proportion of patient population diagnosed with each of psychosis, bipolar disorder, conduct disorder and autism, proportion of patient population comprised of children less than 18 years of age in foster care and proportion of patient population currently taking APs.
2. Patient simulation: Each physician was presented 10 patient profiles, one at a time. All profiles presented a diagnosis of mild, moderate or severe psychosis. The other patient variables such as age, parental concern about use of APs, lab values such as WBC count, ANC count were varied between the profiles in an orthogonal manner. At the bottom of each patient profile, the physician was asked to indicate his/her treatment choice(s) by checking items from a list that included all APs available on the market along with the option for using other classes of products, non-pharmacological treatments and referral to other providers. The patient characteristics provided in each profile and the different levels of each characteristic are presented in Table 1. A sample patient profile in the format presented to respondents is included in Appendix A.
3. Follow-up questions: A few follow-up questions were asked to address key beliefs about the level of evidence for use of AP products. The Evidence Based Practice Attitude Scale (EBPAS) was administered to the respondents as part of the follow-up questions to assess physician's adoption of evidence in their treatment decisions and practice. Physician's beliefs in evidence

supporting use of APs in children, less than 17 years of age, diagnosed with psychosis was also measured.

4. Physician background: In this final section, physician demographics were measured. Variables collected were age, race and gender.

Patient profile development

Development of appropriate patient profiles is an integral part of a patient simulation study. Patient profiles were designed to contain the information needed by physicians in order to make treatment decisions. An initial list of patient attributes that were believed to influence the use of APs was developed from current literature (see chapter 1). The overall goal was to ensure that the combinations of various levels of the patient attributes were composed in a manner that allowed for statistical analysis of the effect of each attribute independently. This was achieved by developing an orthogonal fractional design using the final attributes.

Initially the aim of the study was to assess the prescribing pattern of physicians for children with any mental health disorders, it was decided that a particular diagnosis has to be identified in order to effectively carry out the patient simulation. For this purpose, diagnoses such as psychosis, schizophrenia, autism, ADHD and conduct disorder were considered. However, many of these disorders are hard to diagnose in a patient in a single interaction and difficult to effectively operationalize in a patient profile. Hence, for the sake of a clear and unambiguous description of diagnosis and symptoms, it was decided that psychosis will be used for all patient profiles.

A number of expert interviews were conducted to continuously improve the patient attribute list and the presentation in patient profiles. Experienced pediatricians, psychiatrists and pharmacists specializing in mental health were identified and interviewed face-to-face or via teleconference in order to obtain their input. Three major points of information were gathered from each interview. First, whether the list of patient attributes was complete or if it contained any variables that the physician is not

accustomed to having available during a regular patient visit; second, the most appropriate manner in which the selected attributes could be expressed in text form in a patient profile so that they convey the change in level that is intended; and finally, the ideal arrangement of these attributes on the profile so that and the information is presented in a customary manner and the respondent is not biased to pay more attention to any one attribute than normally would occur. It was also ascertained that none of the attributes or their levels were so extreme that the focus of the patient interaction be diverted away from the initial diagnosis of psychosis. Interviewees were sent copies of the patient profiles and the survey to go through during the development interviews.

Once the list of patient attributes was finalized, the coded levels of each attribute was then expressed in an appropriate text format. Depending on the patient attribute and how the information might typically be presented in a patient chart, each attribute was presented as a bullet point of information in a table or as sentences below the table. The final placement of each of these attributes can be seen in a sample patient profile provided in Appendix A. The attribute levels for the patients were stored in a grid in an Excel spreadsheet. The text expressions of the attributes were created in another worksheet using formulas. The patient profiles used in the survey were generated through the on-line program in a manner similar to that used by mail merge in Microsoft Word, where the text expressions were inserted into a patient chart template.

Profile set

SPSS Orthoplan procedure was used to create an orthogonal combination of levels of attributes to form a set of patients. The orthoplan procedure combines various levels of attributes to produce a set that allows the effect of each variable to be assessed independently during statistical analysis. This procedure produced a set of 27 patient profiles. In order to partition the profiles into equal numbered subsets, 3 hold-out samples were generated to obtain 30 complete patient profiles.

Because the respondent population was particularly susceptible to survey fatigue and time constraints, it was decided that displaying all 30 profiles to each respondent would be overly burdensome. Therefore, the 30 profiles were grouped into 3 subsets of 10 profiles each that were balanced with respect to the hypothesized major drivers of use. Each respondent was shown one subset. The subsets were rotated within each quota group such that each subset was used approximately the same number of times and each patient profile was shown approximately the same number of times within each physician specialty.

Operationalization

Patient factors/attributes: All patient factors were manipulated in the patient profiles displayed to the respondent. A patient name, selected to match patient race and sex, was presented at the top of every profile along with information about the diagnosis of psychosis. The variable foster status (Pt_caregiver) was operationalized as whether consent for use of APs was provided by the patient's 'parent' or 'guardian'. Profiles presented with the word 'guardian' were considered to be foster children. The variable concern about consent (Pt_consent) was operationalized as the level of concern expressed by the caregiver (parent/guardian) while giving consent for use of APs. This was operationalized as '…hasn't expressed any concerns about the use of antipsychotics' or '…has expressed some concern about the use of anti-psychotics" or '…has expressed a lot of concern about the use of anti-psychotics' depending on the level of the variable. Patient adherence (Pt_adherence) was expressed as whether the caregiver mentions that '…the patient takes his medications on time' or '…the patient refuses to take medications'. Alcohol or substance abuse (Pt_Alc) was expressed as either 'The patient has no history of alcohol abuse' or 'The patient has a history of alcohol abuse'. The clinical factors were all expressed in a table underneath the patient name and diagnosis. Patient WBC count (Pt_WBC) was expressed as being normal or low. The actual numbers, 4150 for low and 7300 for normal, were also used to allow the physician to

use their own judgment. Patient ANC count (Pt_ANC) was operationalized in similar to WBC count. The count value of 1300 was used for low and 3900 was used for normal levels. Patient's blood glucose level (Pt_diabetes) was also operationalized similarly. The low glucose level was expressed as 85mg/dl and the normal level was expressed as 112mg/dl.

Patient age (Pt_age) was operationalized to be in one of three categories: 5 years and below (4 years), 6 to 12 years (10 years) and 13 to 17 years (15 years). Values of age were not varied within each group so as to minimize variance to obtain more robust results. Patient race (Pt_race) was operationalized as either Caucasian or African-American. Patient sex (Pt_sex) was expressed as male or female. Patient puberty (Pt_puberty) was expressed as 'pubertal' or 'pre-pubertal'. All of the above variables were mentioned in text clearly in the table below the patient name and diagnosis. Patient BMI (Pt_BMI) was operationalized as being underweight, normal or overweight. The actual numerical values for BMI were obtained from CDC growth charts. Average height of children for the ages of 4 years, 10 years and 15 years for males and females were also obtained from CDC growth charts. With numerical values for BMI and height, weight was computed and all three variables, height, weight and BMI, along with the description of overweight, normal or underweight, were displayed in the table clearly.

Disease severity, with the levels mild, moderate and severe, was expressed both directly at the top of the profile with the diagnosis and again with a description of symptoms directly below the diagnosis. Symptoms used were common for patients of all age groups, so that variability could be minimized during analysis. The set of symptoms used for mild severity were 'occasional uncontrollable agitation, minimally intrusive auditory hallucinations and mild lack of age-appropriate grooming'. For moderate severity, the symptom set 'constant uncontrollable agitation, moderately intrusive auditory hallucinations, moderate lack of age-appropriate grooming' was used and 'constant uncontrollable agitation, severely intrusive auditory hallucinations, severe lack of age-appropriate grooming & some self-harm and harm to others' was used for the severe patients.

Physician factors/attributes: The measurement of various physician factors was done through questions that can be seen in Appendix B. Physician specialty is classified as either PCP or PSYCH and the operationalization is mentioned in the previous section under 'sample'. Years in active practice, mental health patient volume in a typical week, proportion of mental health patient population less 18 years of age in foster care and past use of APs are assessed as self-reported measures in the screener. Similarly, physician age, race and gender were also assessed in the final demographics section of the survey.

The evidence based practice measure was assessed through administration of the Evidence Based Practice Attitude Scale (EBPAS) (Aarons, 2004). The EBPAS is a rather recently developed scale. However, it has been well validated and cited several times in recent years. The scale was used as mentioned by original authors (Aarons, 2004) with all the subscales.

Physician's belief regarding the evidence supporting use of APs in children with mental health disorders was assessed independently through question Q12 (see survey). Response options provided for evidence were (1) labeled indication, (2) medically accepted use but not a labeled indication, (3) no evidence supporting use, (4) no evidence supporting use. The response option 'don't know' was recoded to 'no evidence supporting use' after the data collection phase. Because evidence varies depending up on the product being used and the age of the patient, it was assessed independently for all 11 APs, in each of three age categories: 5 years and under, 6 to 12 years and 13 to 17 years. During analysis, the maximum level of evidence selected by each individual physician for patients in a particular age group was then used as the level of evidence variable for patient profiles of the corresponding age. This operationalization assumes a class effect for the use of AP products in each age group.

Dependent variable: The dependent variable in this study is whether an AP product was prescribed or not. At the end of each profile the respondent was provided an exhaustive list of treatment options. The list of these options can be seen in Appendix A. If the respondent picked any of the AP

products for a given profile, the dependent variable was coded as ‘1’, indicating that APs were prescribed in that scenario

DATA ANALYSIS

The data collected from the survey were analyzed using IBM SPSS (Chicago, Illinois). Data were obtained in the form of an SPSS dataset with respondent ID and responses collected from the each respondent. There were no missing variables since respondents were required to answer all questions in the survey. To ensure data quality, the data were thoroughly vetted qualitatively to make sure responses were all answered carefully and responsibly. It was found that some responses included more treatment options than would be considered possible in a real world setting. In order to clean the dataset, responses with more than three non-AP drugs in two or more patient profiles were deleted.

A regression model was used to meet the research objectives. Since the dependent variable for the study is dichotomous (use/no use of APs) a logistic regression model with a logit link function was determined to be appropriate. However, the structure of the data obtained was such that each physician treated 10 patient profiles. So the treatment decisions made by a given physician were all correlated with each other. Therefore, the data in question do not meet the assumption of independence of observations, which is required to obtain robust results from a logistic regression model. To account for this lack of correlation, marginal modelling using General Estimating Equations (GEE) was employed.

A GEE model takes into account the correlation between responses from the same respondent by treating this correlation as a nuisance variable that can be accounted for during analysis. The correlation matrix was assumed to be ‘exchangeable’, meaning that the correlation between all the responses from the same respondent was assumed to be equal. Because the dependent variable was binomial, a logit link function was used for analysis.

Data management

In order to use a GEE approach, the data needed to be arranged such that SPSS could distinguish the within-subject variables from the between subject variables. The dataset obtained from the vendor was in wide file format with each individual respondent as a single row with all 10 treatment decisions in consecutive columns. This form of data structure was not suitable for running a GEE model. Therefore, the dataset was transposed to a long file format where each respondent had 10 separate observations or rows, with each row containing the treatment decisions for a single patient profile. The patient profiles displayed to each physician were identified by a profile ID assigned to each combination of attributes decided earlier. The levels of each attribute were then obtained from the Excel worksheet that was used to generate the profiles and then merged with the SPSS dataset to make the final dataset that was ready for analysis. To summarize, the final dataset contained 10 observations or rows for each physician. Each of the 10 rows contained the same physician demographics and practice characteristic. Each row also included a patient profile ID and its corresponding attribute levels and the treatment decision(s) made by the physician for that profile.

Data analysis

Since sample size obtained was small, a model building approach was chosen to measure the effects of each variable. (Hosmer & Lemeshow, 2004). All patient and physician variables were entered separately into two models, once with only PCPs, and once with PSYCHs. The variables which were found to be significant at an alpha of 0.1 were then entered together into a final model for each specialty. The significant predictors for each specialty model, at an alpha of 0.05, were then identified and entered into an overall model which included the entire sample. This model was used to test the significance of the interactions of these predictors with physician specialty.

BIBLIOGRAPHY

Hosmer Jr, D. W., & Lemeshow, S. (2004). Applied logistic regression. John Wiley & Sons.

CHAPTER III

DETERMINING PHYSICIAN AND PATIENT CHARACTERISTICS THAT PREDICT THE USE OF ATYPICAL ANTIPSYCHOTICS IN CHILDREN WITH MENTAL HEALTH DISORDERS

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Determining Physician and Patient Characteristics that Predict the Use of Atypical Antipsychotics in Children with Psychosis

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ABSTRACT

Objective: The objective of this study is to determine how patient and physician level factors influence decisions to prescribe atypical antipsychotics to children (under 18years) diagnosed with psychosis.

Methods: This study is a cross-sectional survey of general practitioners and psychiatrists. A web-based patient simulation survey using fractional factorial design was administered with the help of a commercial vendor. Respondents were presented with simulated patient profiles that contained various levels of factors considered to be essential to decision making. Physician treatment decisions were measured along with demographics and beliefs about products. Marginal modelling using General Estimating Equations were used for analysis.

Results: Patient age, disease severity, physician specialty and belief about evidence supporting use of the drug were found to significantly influence physician prescribing decisions.

Conclusions: This study shows that patient age and other factors are important when physicians from different specialties are making decisions about the use of antipsychotics.

Keywords: Atypical antipsychotics, children, psychiatrists, pediatricians, psychosis

DETERMINING PHYSICIAN AND PATIENT CHARACTERISTICS THAT PREDICT THE USE OF ATYPICAL ANTIPSYCHOTICS IN CHILDREN WITH MENTAL HEALTH DISORDERS

Atypical antipsychotics (AP) are approved for use in some children below 18 years of age for diseases such as schizophrenia and bipolar disorder. The use of these drugs has increased exponentially over the past few years (Pathak, West, Martin, Helm & Henderson, 2010). Even though there is limited evidence of the effects of these drugs in children, they are being prescribed for children for several different conditions. Existing studies point toward a range of potential serious adverse events such as weight gain, diabetes, hypertension, metabolic and endocrine abnormalities, hyperprolactinemia, dyslipidemia in the short term and several other unknown long-term effects (Vitiello et al., 2009; McIntyre & Jerrell, 2008; Fedorowicz & Fombonne, 2005; Kumra et al., 2008). With increasing safety concerns and budgetary constraints, payers such as Medicaid have sought to better understand the use of these drugs in children (Surles, 2005; Strawbridge, 2011).

In 2011, a Government Accountability Office (GAO) study examined the rates of use of psychotropic medication among foster children in several state Medicaid programs and recommended to the Department of Health and Human Services that they should provide guidance to states on best practices for overseeing psychiatric prescriptions (Kutz, 2011). In response to this, the Department of Health and Human Services (DHHS) sent a letter to the state directors making them aware of the growing problem of safe, appropriate and effective use of

psychiatric prescriptions among foster children. They proposed an expansion of activities and collaboration between the Administration for Children and Families (ACF), the Center for Medicare and Medicaid Services (CMS) and the Substance Abuse and Mental Health Services Administration (SAMHSA) (DHHS, personal communication, November 23, 2011).

The increasing recognition from the FDA and the DHHS demonstrates the importance of addressing the issue of use of APs in children. This study aims to help understand the process of prescription decisions better so all of the players in the health care system can plan for better ways to assure more efficient and safer use of APs in children and adolescents. The objective of this study is to identify the patient and physician level factors that most influence physicians' decisions to prescribe APs in children and adolescents less than 18 years of age

LITERATURE REVIEW

Use of atypical antipsychotics

Cooper et al. (2006) found that the use of APs for approved indications grew 2.49 times between the periods 1995-1998 and 1999-2002, while the use for the unapproved indications grew 3.52 times. Interestingly, the article also concluded that 30% of all antipsychotic prescriptions were attributable to non-psychiatrists. Evidence available from an expert panel convened by the European Neuro-psychopharmacology, to study efficacy and safety data, states that children and adolescents are more vulnerable to side-effects from APs than are adults (Vitiello et al., 2009). Research suggests that some risk factors may be associated with children's susceptibility to the side-effects of these drugs. McIntyre and Jerrell (2008), studying the pattern of adverse events associated with the use of APs in children and adolescents in the South Carolina Medicaid database, found that children treated with these drugs have the risk of acquiring diseases such as obesity, type II diabetes, dyslipidemia and orthostatic hypotension among others.

Olfson, Blanco, Liu, Moreno & Laje (2006) conducted research into various patient characteristics related to AP use. They found that more males receive APs than do females; and that children insured by Medicaid are prescribed more APs than privately insured children. While the reasons for this differential use have not been established by research, many of these patterns have been documented in multiple studies (Olfson et al., 2006; Hamann, Langer, Leucht, Busch & Kissling, 2004; Pathak et al., 2010).

The letter sent to the Medicaid state directors from the Department of Health and Human Services mentions that factors such as age, gender, behavioral concerns and placement type (for foster children) can affect likelihood of being prescribed psychotropic medications (DHHS, personal communication, November 23, 2011; Strawbridge, 2011).

Prescription decisions

The study of prescription decision making has been well researched over the years. Some researchers have compared the act of prescribing to an art that goes beyond mere pharmacological factors. It has been called a complex skill that requires the physician to carefully evaluate the patient's physical, psychological, social and behavioral illnesses and weigh the benefits and risks of each treatment alternative and comparing it to the option of not treating the indication (Howie, 1976).

There is also a lot of evidence to suggest that prescription decision making is not dependent only upon clinical factors. In his study on antibiotic use in cases of sore throat, Howie (1976) demonstrated that social and psychological information about the patient can substantially influence prescription decisions. Bradley (1992a), in an attempt to study uncomfortable prescription decisions, found that any prescription decision involving concern about toxicity, failure to live up to expectations, concern about appropriateness and uncertainty caused discomfort among physicians. It seems many of these conditions apply directly to APs.

In an experimental study conducted in Peru, researchers concluded that knowledge about disease seems to make very little difference as to what the physician prescribes. They describe the decision making process as social and not logical. They identified a few important social factors such as the physician's role as a socially defined good practitioner, previous experiences

with diarrhea cases and sometimes even deficiencies in knowledge (Paredes, De La Pena, Flores-Guerra, Diaz & Trostle, 1996).

In another study, researchers found that the physicians' perceptions of patients' expectations influenced prescribing behavior the most. Other factors such as the patient's age, ethnic group and symptoms also influence prescribing behavior. They showed that the physician's perception of the patient's expectations in turn seemed to depend on the patient's symptoms, complaints, age and even on the physician's own qualifications. The study essentially pointed out the importance of patients' social variables in making prescription decisions (Britten & Ukoumunne, 1997). Bradley (1992b) characterized a list of factors influencing prescribing decisions into three general categories: patient factors, physician factors and physician concern about drugs or product factors. He found that several psychotropic drugs and psychiatric conditions were associated with discomfort when prescribing. The current study attempts to identify the specific patient and physician factors influencing prescribing of APs in children with psychosis.

RESEARCH OBJECTIVES

This study has two specific objectives: First, to determine how patient level factors, such as age, race, sex or attitude about consent from parent/guardian influence physicians' decisions about prescribing atypical antipsychotics in children under 18 years of age. Second, to determine how physician characteristics, such as specialization, mental health patient volume or beliefs about drugs influence physician's decision to prescribe APs in children under 18 years of age.

METHODS

Study design and data collection

The study is a cross-sectional survey of Psychiatrists (PSYCHs) and Primary Care Practitioners (PCPs). General psychiatrists and child psychiatrists were classified as PSYCHs, and family medicine, internal medicine, general practice and pediatricians were classified as PCPs. A stratified quota sample of physicians was drawn for the purpose of this study. The sample was be obtained through a national physician panel maintained by Reckner Healthcare, a commercial vendor. Physicians were required to go through a small set of screening questions to make sure they met the inclusion criteria for the study. To be eligible for the study, physicians had to be engaged in full-time active practice for at least 2 years post-residency and spend a majority of their time in the outpatient care setting (50% for PCPs and 25% for PSYCHs). Physicians were excluded from the survey if their practice did not include any mental health patients under 18 years of age, any patients with a diagnosis of psychosis or any patients taking APs.

Survey design

A patient simulation was performed to best replicate actual treatment decisions. Each physician was presented a set of patient cases/profiles with information about demographics, symptoms, clinical parameters and other relevant information. The respondent then chose a treatment plan for each patient from a list of exhaustive options. The information presented in

each profile was carefully constructed, from current literature, to include variables that were expected to be relevant to decision making. Several one-on-one interviews were conducted with psychiatrists, pediatricians and mental health pharmacists to finalize the patient attributes. The list of variables that were present on the profiles and their various levels are presented in Table 1. An orthogonal design was used to find the combinations of various levels of these patient attributes that would support statistical analysis of the effect of each attribute independently. A total of 30 profiles were created out of the combination of variables listed. (See Appendix A for a sample patient profile).

Each respondent viewed one of three randomized blocks containing only 10 out of the 30 profiles. Each block of profiles was balanced with respect to age of patients and disease severity. The survey also contained the Evidence Based Practice Attitude Scale (Aarons, 2004), measures of physician background, practice characteristics and beliefs about evidence supporting use of atypical antipsychotics in children with psychosis.

Physician's belief about evidence concerning use of atypical antipsychotics in children with psychosis was measured by asking respondents their beliefs about the level of evidence that existed for use of the 11 atypical antipsychotics for the three age categories presented in the patient profiles. The level of evidence categories were 'labeled indication', 'medically accepted use but not a labeled indication', or 'no evidence supporting use'. Respondents could also indicate they 'don't know'. The maximum level of evidence found for any atypical antipsychotic was used for the corresponding age group. Full approval for the study was obtained from the University of Mississippi Institutional Review Board prior to data collection.

DATA ANALYSIS

The data collected from the survey was analyzed using IBM SPSS (Chicago, Illinois). Physician treatment choice was modelled using marginal modelling using Generalized Estimating Equations (GEE), with a logit link function, to account for the lack of independence in the dataset. Model building was done in multiple steps (Hosmer, & Lemeshow, 2004). Potential physician and patient factors were introduced in separate models, once for the PCPs and once for PSYCHs. The factors that were found to be significant (alpha ≤ 0.1) were then introduced in the respective PCP and PSYCH overall models. A final model included both specialties while testing for interaction of physician specialty with significant predictors in the PCP and the PSYCH models.

RESULTS

In all, the contracted vendor provided the researchers with 215 completed surveys. Of all respondents who attempted the survey about 50% met the qualifying criteria set by the researchers. The average respondent took about 19 minutes to complete the survey. To ensure data quality, the researchers, after thorough analysis of response patterns, deleted from the final dataset respondents that prescribed more than three non-AP drugs in two or more patient profiles. A total of 193 respondents, or 1,930 unique physician-patient combinations, were used in the analyses.

Physician characteristics

Summaries of respondent demographics and beliefs are provided in Tables 2 and 3. All physicians were classified as either Primary care practitioners (PCPs) or Psychiatrists (PSYCHs) based on their specialization. The final dataset for analysis contained 129 respondents classified as PCPs and 64 classified as PSYCHs.

The mean age of PCPs in the final dataset was 50.2 years and the mean age of PSYCHs was 54.1 years. The respondents were composed of 17.2% females; 63% Caucasians and 27% Asian Americans. Distribution within race and gender was similar across the specialties. Given the distribution obtained, the race variable was recoded as Caucasian, Asian American or other, in order to reduce correlation between independent variables in the final model.

PSYCHs were found to be significantly older, have spent more years in active practice, have higher patient volume in a typical week, and have a higher percentage of patients who are foster children. In line with expectations, PCPs were found to spend a significantly greater proportion of their time in outpatient care (92% versus 80% for PSYCHs). On the evidence based practice attitude scale, which measures the extent of evidence driven practice behavior, it was found that PSYCHs had significantly higher scores on the overall score and the openness subscale (subscale 3) (see Table 3).

Prescribing patterns

Across all physicians and patient profiles, 1,930 (71.2%) patients were treated with APs (Table 4). Significant difference in prescribing patterns between PCPs and PCYCHs were observed for prescribing of APs and referrals to another physician. PCPs were more likely to refer the patient to another physician (50% vs 16% for PSYCHs) and less likely to prescribe APs themselves (63.6% for PCPs vs 86.6% for PSYCHs). Further, PCPs were also significantly less likely to prescribe psychosocial therapy to their patients (44% vs 55% for PSYCHs).

Factors influencing prescribing behavior

GEE models were used to identify factors that influences prescribing behaviors. Complete results from these models are shown in Table 5.

It was found that belief about evidence supporting use of APs, patient disease severity and patient age significantly predicted prescription behavior among both PCPs and PSYCHs. PCPs and PSYCHs differed significantly in their prescribing behavior with changes in patient WBC count, disease severity, proportion of patient population diagnosed with psychosis and the proportion of patients using APs.

DISCUSSION

The results of this study point out that there are considerable differences between the practices of PCPs and PSYCHs. PSYCHs were more likely than PCPs to prescribe APs for young patients. This finding is along the same lines as Cooper et al. (2006) who found that increase in frequency of use of APs by 'mental health providers' was more than twice the increase seen in 'non-mental health providers'. Since a large percentage of children with mental health problems are treated by PCPs, it is important to understand these differences and how they might affect the quality of care received by children. These differences might arise due to a large number of reasons, some of which were identified in this study.

Patient characteristics

The important patient characteristics that best predicted prescribing of APs were age and disease severity. It appeared that patients were more likely to be prescribed atypical antipsychotics when their disease was severe or moderate, in comparison to mild severity. This is in line with the expectation that increasing severity requires immediate and intensive therapy (Gleason et al, 2007). Among PSYCHs, the odds ratio for moderate patients is approximately 2.54 (95% CI = 1.626-3.961), whereas that for the severe patients is 3.51 (95%CI = 1.870-6.530). Although PCPs were more likely to prescribe APs as severity went up, they did not differentiate between moderate and severe patients the way PSYCHs did. The odds ratio for PCPs for mild to moderate patients was 1.35 (95% CI = 1.023-1.017) and for mild to severe was 1.29 (95% CI = 0.917-1.814). The difference in responses to severity level was significant as

shown by the interaction of specialty with disease severity. This might be explained by the fact that PCPs may not be as comfortable treating patients with increased severity and preferred to refer such patients to specialists. This interpretation is supported by the increased rate of referrals as shown in Table 4 (50% for PCPs vs 16% for PSYCHs). Documented expert interviews corroborate the hypothesis that most PCPs are likely to refer patients as soon as psychotic symptoms are identified (Sussman, 2008).

As expected, changes in prescription patterns were associated with changes in patient age. Physicians prescribed fewer APs to younger children, with an odds ratio of 0.32 (95% CI = 0.212 - 0.476) for 4 year olds and 0.69 (95% CI = 0.534 – 0.880) for 10 year olds when compared to 15 year olds. Pathak et al. (2010) also found that use of APs increases with increases in patient age. Prescription patterns among PCPs and PSYCHs did not significantly with respect to changes in patient age.

Patients with abnormally low WBC counts were found to be significantly less likely ($p < 0.05$) to be prescribed APs. Normal values of patient WBC count did not predict prescription behavior in the model for the PSYCHs (OR = 0.65; 95% CI = [0.412-1.029]), but was significant in the model for PCPs (OR = 1.37; 95% CI = [1.129-1.668]). The significance of WBC count in treating children with mental health disorders is not unheard of in published literature. WBC values are suggested for constant monitoring (every 2 or 4 weeks), especially if the patient is using clozapine, because it has a blackbox warning listed for agranulocytosis (Texas Department of Family and Protective Services, 2010; Gasper & Tsai, 2006). While this effect does not seem to exist across all atypical antipsychotics, it still seems to drive prescription behavior among PCPs.

Not all APs have labeled indications for use in young children with psychosis; therefore, the level of parent or guardian concern when providing consent for their use was hypothesized to be a factor influencing decisions about using APs in the study (Strawbridge, 2011). Parent or guardian's concern about use of APs and patient's foster status (foster child or not) were not found to be significant predictors. These factors failed to meet the alpha of 10%, in the initial models for each physician type and thus were not included in the final models. Patient sex, race, BMI, puberty status, alcohol use and blood glucose levels also did not meet the criteria for inclusion in the models for each physician type. It was surprising that none of these factors were significant predictors, because literature presents some contrasting evidence. For example, weight gain is a significant side effect with most APs and monitoring patient's BMI is recommended by several guidelines (Texas Department of Family and Protective Services, 2010; Gasper & Tsai, 2006; Culpepper, 2007; Teicher & Glod, 1990; Varley & McClellan, 2009). Similarly, monitoring puberty or sexual function is also recommended by guidelines for prescription of APs (Texas Department of Family and Protective Services, 2010).

The studies which highlight the disproportionately high use of APs in foster children, suggest that this might be because of greater exposure to trauma, frequent changes in foster placement and varying state oversight policies (Kutz, 2011; Strawbridge, 2011; Zito et al., 2008). The finding that physicians are no more likely to prescribe these drugs to foster children provides evidence that increased use of atypical antipsychotics in foster children is driven by clinical factors and not on foster status of the child. A similarly positive finding is the non-significance of the factor 'parental concern'. This finding reinforces the belief that physician decisions are driven more by objective clinical criteria.

Physician characteristics

As previously discussed in the results section, the most important physician characteristic was specialty. Cooper et al. (2006) found similar results in their study on trends in prescription of APs using data from the National Ambulatory Medical Care Survey and the National Hospital Ambulatory Medical Care Survey.

Only one other physician factor, belief about evidence supporting use of APs, was found to be a significant predictor ($p < 0.001$) among both PCPs and PSYCHs. This variable was measured separately for each specific patient age category for the psychosis diagnosis. Physicians prescribed significantly more atypical antipsychotics when they believed there was evidence to support use, either labeled or medically accepted.

The proportion of patient population diagnosed with psychosis (OR = 0.96; 95% CI = [0.933-0.987]; $p < 0.01$) and the past use of APs (OR = 1.04; 95% CI = [1.014-1.062]; $p < 0.01$) were also found to significantly predict PSYCH prescribing behavior, but not PCP behavior. However, as shown by the odds ratios and the confidence intervals, these ratios are barely significant and the magnitude of the ratios indicates they do not have a meaningful impact on prescribing decisions.

Limitations

This study provides valuable contributions to our understanding of decisions related to prescribing APs for children. As with any study, however, there are a few limitations that need to be considered. A national panel of physicians was used for this study. A summary of the study results was offered as the only incentive for participation. There exists a potential risk for non-response bias since the only incentive was information about the results. The sample obtained

was skewed in terms on distribution for race (majority Caucasians and Asian Americans) amd gender (17% female) which could further limit generalizability of the findings. The low sample size also resulted in an underpowered study, especially for PSYCHs. This could have resulted in missing other effects which might have been significant predictors of prescribing decisions. This study used the diagnosis of psychosis in its patient profiles. Generalizations to other mental health conditions in children must be made with caution.

Further, even though patient simulation was used to capture treatment decisions, it is not possible to capture to the actual decisions made during patient visits other than through chart reviews. The patient profiles were revised several times to provide the information a physician would have and need during a regular office visit for this type of patient. However, respondents were not able to acquire additional information they may have felt was needed. Since the patient simulation process does closely replicate the actual decision making process in practice, this bias, if present, was considered to be minimal.

CONCLUSIONS & FUTURE STUDY

Clinical Relevance

This study shows that physicians' prescribing of APs in children with psychosis is heavily influenced by factors such as patient age, disease severity, physician specialty and belief about evidence supporting use of the drug. More importantly, this study demonstrated differences in prescribing behaviors for PCPs and PSYCHs when treating the same patients.

This study can provide guidance for strategies for assuring clinically appropriate and safe use of antipsychotics in children. For both types of physicians, patient age and disease severity were significant factors in treatment decisions. This indicates that most physicians are appropriately considering clinical factors. Overall, physicians were significantly influenced by their beliefs about evidence based prescribing. This is important in that it indicates that education about clinical appropriateness will influence prescribing of APs.

Future study

While this study contributes to the pediatric psychology literature, there is a lot of scope for further research. The present study only deals with children of ages 4, 10 and 15 years with psychosis, and cannot be generalized to all mental health conditions in children under 18 years. The most common conditions observed in children today are ADHD, Autism, Oppositional Defiant Disorder, etc. These diseases can be much more challenging to diagnose and are also liable to overprescribing. The factors influencing prescriptions in these disease states also need to

be better understood, since they account for a large percentage of the use of APs in children today.

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BIBLIOGRAPHY

Bradley CP. Uncomfortable prescribing decisions: a critical incident study. *BMJ*. 1992a; 304:294-296.

Bradley CP. Factors which influence the decision whether or not to prescribe the dilemma facing general practitioners. *Brit Gen J Pract*. 1992b; 42:454-458.

Britten N, Ukoumunne O. The influence of patient's hopes of receiving a prescription on doctor's perceptions and the decision to prescribe: a questionnaire survey. *BMJ*. 1997; 315:1506-1510.

Cooper WO, Arbogast PG, Ding H, Hickson GB, Fuchs C, Ray WA. Trends in prescribing of antipsychotic medications for US children. *Ambul Pediatr*. 2006; 6:79-83.

Crystal S, Olfson M, Huang C, Pincus H, Gerhard T. Broadened use of atypical antipsychotics: Safety, effectiveness and policy challenges. *Health Affair*. 2009; 28(5): 770. Available at: http://content.healthaffairs.org/content/28/5/w770.full.html

Cullen KR, Kumra S, Regan J, Westerman M, Charles SC. Atypical Antipsychotics for treatment of schizophrenia spectrum disorders. Psychiatric Times. 2008; 25 (3):2.

Department of Health and Human Services, Letter to State Director. Washington DC: 20201.

Domino ME, Swartz MS. Who are the new users of antipsychotic medications? *Psychiatr Serv*. 2008; 59:507–514.

Fedorowicz VJ, Fombonne E. Metabolic side-effects of atypical antipsychotics in children: a literature review. *J Psychopharmacol*. 2005; 19(5):533-550.

Hamann J, Langer B, Leucht S, Busch R, Kissling W. Medical decision making in antipsychotic drug choice for Schizophrenia. *Am J Psychiatry*. 2004; 161:1301-1304. Harris CM. Personal view. *BMJ*. 1980; 280:57.

Hosmer Jr, D. W., & Lemeshow, S. (2004). *Applied logistic regression*. John Wiley & Sons.

Howie JR. Clinical Judgment and antibiotic use in general practice. *BMJ*. 1976; 2:1061–1064.

Kumra S, Oberstar JV, Sikich L, Findling RL, McClellan JM, Vinogradov S, Schulz SC. Efficacy and tolerability of second-generation antipsychotics in children and adolescents with schizophrenia. *Schizophrenia Bull*. 2008; 34(1):60-71.

Kutz GD. Foster children: HHS guidance could help states improve oversight of psychotropic prescriptions. Washington DC: General Accounting Office Report GAO – 12- 270T.Farah A. Atypicality of atypical antipsychotics. *Prim Care Companion J Clin Psychiatry*. 2005;7:268-274.

Olfson M, Blanco C, Liu L, Moreno C, Laje G. National trends in the outpatient treatment of children and adolescents with antipsychotic drugs. *Arch Gen Psychiatry*. 2006; 63:679-685.

Malone R, Sheikh R, Zito J. Novel antipsychotic medications in the treatment of children and adolescents. *Psychiatr Serv.* 1999;50(2): 171-174.

McIntyre RS, Jerrell JM. Metabolic and cardiovascular adverse events associated with antipsychotic treatment in children and adolescents. *Arch Pediatr Adolesc Med*. 2008; 162 (10):929-935.

Paredes P, De La Pena M, Flores-Guerra E, Diaz J, Trostle J. Factors influencing physician's prescribing behavior in the treatment of childhood diarrhea: Knowledge may not be the clue. *Soc. Sci. Med.* 1996; 42(8):1141-1153.

Pathak P, West D, Martin BC, Helm M, Henderson C. Evidence-based use of second generation antipsychotics in a state Medicaid pediatric population, 2001 – 2005. *Psychiatr Serv.* 2010;61 (2): 1–7.

Staller JA, Wade MJ, Baker M. Current prescribing patterns in outpatient child and adolescent psychiatric practice in New York. *J Child Adolesc psychopharmacol.* 2005; 15:57-61.

Surles RC. Atypical antipsychotics: Considerations for Medicaid coverage. *Am J Managed Care*. 2005; 11(8):S248-S253.

Texas Department of Family and Protective Services; University of Texas at Austin College of Pharmacy. (2010, December) Psychotropic Medication Utilization Parameters for Foster Children. Retrieved from: http://www.dfps.state.tx.us/Child_Protection/Medical_Services/guide-psychotropic.asp

Vitiello B, Correll C, van Zwieten-Boot B, Zuddas A, Parellada M, Arango C. Antipsychotics in children and adolescents: Increasing use, evidence for efficacy and safety concerns. Eur.Neuropsychopharmacol. 2009.04.008.

LIST OF APPENDICES

APPENDIX A: TABLES

Table 1: List of Patient Attributes

VARIABLE NAME	VARIABLE DESCRIPTION	VARIABLE LEVELS		
		0	**1**	**2**
Pt_severity	Disease severity	Mild	Moderate	Severe
Pt_Adherence	Risk for non-adherence	Absent	Present	-
Pt_WBC	WBC count	Low	Normal	-
Pt_ANC	ANC count	Low	Normal	-
Pt_Alc	Alcohol / Substance abuse	No	Yes	-
Pt_BMI	BMI	Underweight	Normal	Overweight
Pt_Sex	Sex	Male	Female	-
Pt_Race	Race	Caucasian	Black	-
Pt_Age	Age	<5	6 – 12	13 – 17
Pt_Puberty	Puberty	No	Yes	-
Pt_Caregiver	Type of caregiver	Parent	Guardian	-
Pt_Diabetes	Type 2 Diabetes mellitus	No	Yes	-
Pt_Consent	Concern about consent	None	Medium	High

Table 2: Respondent demographics

Variable	Physician specialty	
	PCP (N = 129)	PSYCH (N = 64)
Age**	50.28 (7.957)	54.17 (8.759)
Females#	22 (17.1)	11 (17.2)
Race#		
Caucasians	80 (62.0)	42 (65.6)
Asian Americans	36 (27.9)	16 (30.8)
African Americans	2 (1.6)	0 (0)
Native Hawaiians	1 (0.8)	0 (0)
Hispanics	3 (2.3)	0 (0)
Others	7 (5.4)	6 (9.4)
Years in practice*	17.99 (6.945)	20.17 (7.030)
Patient volume per week***	174.55 (122.654)	108.30 (74.485)
% of patients in foster care**	9.08 (11.770)	15.95 (17.100)
% of patients using atypical antipsychotics	27.39 (26.531)	35.05 (24.393)
Proportion of time spent in		

Inpatient care**	6.37 (10.694)	14.80 (18.871)
Outpatient care***	92.00 (12.094)	80.03 (21.743)
Administration*	1.16 (2.561)	2.69 (4.757)
Teaching/Research	.47 (1.719)	2.48 (6.512)
Proportion of patients diagnosed with		
Psychosis**	10.83 (12.624)	18.33 (16.588)
Bipolar disorder*	17.73 (16.155)	23.16 (13.046)
Conduct disorder**	29.53 (27.028)	20.52 (14.573)
Autism	11.95 (13.358)	13.63 (11.928)
Proportion of age groups		
5 and under	4.02 (5.750)	4.59 (7.849)
6 to 12 years**	8.46 (8.203)	13.56 (14.115)
13 to 17 years	15.79 (11.813)	18.03 (10.936)
18 and over*	71.74 (21.481)	63.81 (27.675)
Profiles who were prescribed atypicals	820 (63.6)	554 (86.6)

All values are Mean(Standard Deviation); except # (N and percent);
*** - $p < 0.001$; ** - $0.001 < p < 0.01$; *- $0.01 < p < 0.05$;

Table 3: Physician beliefs about evidence for use of atypical antipsychotics

Variable	Physician specialty	
	PCP (N = 129)	PSYCH (N = 64)
Physician's belief about evidence for use of AP in children 5 years and under		
Medically accepted use	17 (13.2)	14 (21.9)
No evidence	45 (34.9)	27 (42.2)
Don't know	33 (17.1)	13 (6.7)
Physician's belief about evidence for use of AP in children between 6 and 12 years*		
Labelled indication	24 (18.6)	6 (9.4)
Medically accepted use	8 (6.2)	6 (9.4)
No evidence	48 (37.2)	17 (26.6)
Don't know	49 (38)	35 (54.7)
Physician's belief about evidence for use of AP in children between 13 and 17years		
Labelled indication	15 (11.6)	3 (4.7)
Medically accepted use	2 (1.6)	2 (3.1)
No evidence	36 (27.9)	13 (20.3)
Don't know	76 (58.9)	46 (71.9)
Evidence Based Practice Attitude Scale (EBPAS)[#]		
Requirement	1.83 (1.068)	1.93 (1.071)
Appeal	2.47 (.784)	2.68 (.621)
Openness**	2.07 (.864)	2.46 (.816)
Divergence	2.457 (.875)	2.34 (.890)
Total	2.21 (0.480)	2.35 (0.483)

All values are N and percent; except #: Mean(Standard Deviation);
EBPAS and subscales are scored on a scale of 0 to 4.
*** - $p < 0.001$; ** - $0.001 < p < 0.01$; *- $0.01 < p < 0.05$;

Table 4: Prescribing patterns across all profiles displayed

Treatment	Physician specialty	
	PCP	PSYCH
Atypical Antipsychotics		
5 years an under***	45.99	74.66
6 to 12 years***	67.22	91.19
13 to 17 years***	78.29	94.79
All age groups***	63.57	86.56
Other pharmaceutical treatment		
5 years and under	30.42	31.67
6 to 12 years	45.51	40.53
13 to 17 years	45.99	41.67
All age groups	40.7	37.81
Psychosocial treatment		
5 years and under***	38.92	60.18
6 to 12 years*	46.35	54.19
13 to 17 years	48.32	52.08
All age groups***	44.5	55.63
Referral to another physician		
5 years and under***	59.91	23.53
6 to 12 years***	47.81	15.42
13 to 17 years***	42.64	10.42
All age groups***	50.23	16.72

All numbers are expressed as a percentage of the total population in that age group
*** - $p < 0.001$; ** - $0.001 < p < 0.01$; *- $0.01 < p < 0.05$;

Table 5: Comparison of factors influencing physician prescription of atypical antipsychotics in three models

	Physician specialty OR (95% CI)	
Characteristics	PCP	PSYCH
Psychiatrists	0.328 (0.012 – 9.259)	
Physician's belief about evidence supporting use		
Labelled indication	5.70 (3.034-10.707)***	
Medically accepted use	3.70 (1.949-7.023)***	
Physician Race		
Asian American	1.257 (0.553 -2.859)	
Caucasians	0.819 (0.376- 1.785)	
Proportion of patients diagnosed with psychosis	1.01 (0.989 – 1.024)	0.96 (0.933-0.987)**
Proportion of patients using atypicals	1.01 (0.995 – 1.017)	1.04 (1.014-1.062)**
Years spent in active practice	1.031 (0.990-1.074)	
Patient severity		
Severe	1.29 (0.917-1.814)	3.51 (1.870-6.530)***
Moderate	1.35 (1.023-1.783)*	2.54 (1.626-3.961)***
Patient age		
4 years	0.32 (0.212 – 0.476)***	
10 years	0.69 (0.534 – 0.880)**	
Patient WBC Count (Normal range)	1.37 (1.129-1.668)**	0.65 (0.412-1.029)
Patient ANC count (Normal range)	0.924 (0.755 – 1.131)	

*** - $p < 0.001$; ** - $0.001 < p < 0.01$; *- $0.01 < p < 0.05$;

Separate odds ratios are provided for PCPs and PSYCHs wherever the interaction between them is significant at the 0.05 level.

Reference category - Psychiatrists: PCPs; Evidence supporting use: No evidence available; Physician Race: Other; Patient severity: Mild; Patient age: 15 years; Patient WBC count: Low WBC count; Patient ANC count: Low ANC count; Patient adherence: Non-adherent.

CHAPTER IV

CONCLUSIONS

SUMMARY & CONCLUSIONS

This study shows that physician prescribing of APs in children with mental health disorders can be predicted based on factors such as patient age, disease severity, physician specialty and beliefs about evidence supporting use of the drug. It provides valuable insight into the prescription decision making process. It helps understand the characteristics that are important to physicians when they make a prescription decision. More importantly, this study showcases the differences in prescribing behaviors of PCPs and PSYCHs and goes further to explain what might drive these differences.

This information is valuable for policy makers trying to assure safe and effective use of APs in children. It provides an understanding for State Medicaid directors and other payers who might be trying to control rising costs, while not jeopardizing rational care. Because it explains the differences between PCP and PSYCH prescribing patterns, it might be possible to put in place step edits or prior authorizations or other such mechanisms tailored to the prescribing physician.

The effect of the belief about evidence, can help formulate a strategy for policy makers to curtail inappropriate use. If physicians can be educated about drug labelling status and acceptable medical use for each AP for specific age categories and diagnoses, it will encourage use only in indications approved by the FDA. Further, because PCPs were found to be prescribing fewer atypicals than PSCYHs and they often indicated referral of patients to specialists, these physicians are probably less knowledgeable about or comfortable with prescribing APs, especially for children. It may be important to have patients managed by these physicians routinely evaluated by a qualified child psychiatrist or other appropriate person in order to assure appropriate use. Some states, such as Florida, require all physicians to obtain a standardized written consent from the parent or guardian before a psychotropic drug is administered

(Kutz, 2011). While this might still contribute toward standardized data collection, this study shows that any concern that a parent or guardian might express during this interaction does not significantly influence physician treatment decisions.

This study also helps pharmaceutical marketing managers who are trying to introduce a product in this market. The study establishes the value a labelled indication holds in this market. Currently, only Abilify, Zyprexa, Seroquel, Invega and Risperidal are approved for treatment of schizophrenia in the age group 13 to 17 years. Abilify and Risperidal are also approved for treatment of irritability associated with autistic disorder in children of ages 6 to 17. It is apparent that approved indications in this market are rare. Several other indications, which are growing in the past decade do not have any approved treatments. This study shows that pharmaceutical companies who are aiming to capture the child and adolescent market in APs need to get the indication approved or establish their product as an acceptable medical use. Although physicians may generalize the level of evidence to the class of products, clinical edits at time of prescription adjudication can easily limit use to appropriate levels of evidence.

Future Research:

While this study contributes to the pediatric psychology literature, there is a lot of scope for further research. The present study only deals with children with psychosis and cannot be generalized to all mental health conditions in children. Diseases such as ADHD, Autism, and Oppositional Defiant Disorder are being commonly diagnosed in children (Pathak et al., 2010). These disease can be much more challenging to diagnose in a single clinic visit and also highly liable to overprescribing. The factors influencing prescriptions in these disease states also need to understood, since they account for a lot of use of antipsychotics today. Further research is also needed to understand how physician decision making is influenced by changes in regulatory framework in order to understand which form of regulation is best suited in order to curb over utilization of APs.

Acknowledgements:

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BIBLIOGRAPHY

.

Kutz GD. Foster children: HHS guidance could help states improve oversight of psychotropic prescriptions. Washington DC: General Accounting Office Report GAO – 12- 270T.Farah A. Atypicality of atypical antipsychotics. *Prim Care Companion J Clin Psychiatry*. 2005;7:268-274.

Pathak P, West D, Martin BC, Helm M, Henderson C. Evidence-based use of second generation antipsychotics in a state Medicaid pediatric population, 2001 – 2005. *Psychiatr Serv.* 2010;61 (2): 1–7.

LIST OF APPENDICES

APPENDIX A: SAMPLE PATIENT PROFILE

(102) Elizabeth:

Doctor, please assume that Elizabeth is a patient you have newly diagnosed with mild psychosis. Her history and your current evaluation notes are summarized below.

Demographics	Lab values	Symptoms
Age: 15 Gender: Female Height: 63.7 inches Weight: 119.5 pounds BMI: 20.7 (Normal) Pubescent Caucasian	WBC: 7300 (Normal) ANC: 1300 (Low) Fasting glucose: 85mg/dL	Patient has displayed symptoms of mild psychosis: • Occassional uncontrollable agitation • Minimally intrusive auditory hallucinations • Mild lack of age-appropriate grooming

The patient's diagnosis is consistent with family history. You have informed the parent about the use of atypical antipsychotics. The patient can afford her drugs.
During the visit you determine that:

- The parent is willing to sign an informed consent and hasn't expressed any concerns about the use of antipsychotics.
- The patient has no history of alcohol abuse.
- The parent mentions that the patient takes her medications on time.

Treatment options: (Please check all that apply)

Atypical Antipsychotics

☐ Aripiprazole (Abilify®)
☐ Asenapine (Saphiris®)
☐ Clozapine (Clozaril®, generic)
☐ Iloperidone (Fanapt®)
☐ Lurasidone (Latuda®)
☐ Olanzapine (Zyprexa®, Zyprexa Relprevv®, generic)
☐ Olanzapine & Fluoxetine (Symbyax®, generic)
☐ Paliperidone (Invega®, Invega Sustena®)
☐ Quetiapine (Seroquel®, Seroquel XR®, generic)
☐ Risperidone (Risperidal, Risperidal Consta®, generic)
☐ Ziprasidone (Geodon®, generic)

Conventional Antipsychotics

☐ Perphenazine (Trilafon®, generic)
☐ Chlorpromazine (generic)
☐ Others

Anti-convulsants

☐ Lithium (Lithobid®, generic)
☐ Alpha agonists
☐ Other

☐ **Anti-depressants**

☐ **Anxiolytics**

☐ **Mood stabilizers**

☐ **Stimulants**

☐ **Other (Please specify _____)**

☐ **Psychosocial Intervention**

☐ **Refer to another physician with experience in dealing with pediatric mental health**

☐ **Refer to non-medical practitioner**

☐ **Other non-pharmaceutical treatment**

APPENDIX B: SURVEY INSTRUMENT

COVER LETTER:

J. Reckner Associates is helping the University of Mississippi conduct a research study regarding the use of antipsychotics in children with mental health disorders as part of a graduate student thesis project. We request your participation in this study.

A few points to note:

- The survey is expected to take approximately 40 – 45 minutes to complete.
- As always your responses will be held confidential.
- The identities of the respondents will not be made available in any form to the research team at the University of Mississippi.
- This study has been reviewed and approved by the University of Mississippi Institutional Review Board (IRB). The IRB has determined that this study fulfills the human research subjects' protection 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 (662)915-7482.
- Your response is of great importance to us. As an academic project, we are unable to offer you an honorarium. However, to show our appreciation for your time, respondents will be sent a summary report of the results from the study by Reckner Associates after the analysis has been completed.

The survey will available only for a limited time. Please complete the survey as soon as possible.

Please click on the following link to enter the survey.

[ENTER LINK]

Thank you for your cooperation.

Best regards.

INTRODUCTION MESSAGE:

Welcome to our study, Doctor. The aim of this study is to understand the use of antipsychotics in children suffering from mental health illnesses.

Please answer the next few questions to determine if you meet the criteria for inclusion in our study.

SCREENER:

1. Which area of specialization best describes your practice?
   (1) Family practice (PCP)
   (2) Internal medicine (PCP)
   (3) Pediatrician (PCP)
   (4) General practice (PCP)
   (5) General Psychiatrist (PSYCH)
   (6) Child and adolescent psychiatrist (PSYCH)
   (7) Other (DISQUALIFY)

2. Are you engaged in full-time active practice?
   (1) Yes
   (2) No (DISQUALIFY)

3. For how many years have you been in practice, post-residency? _____ (DISQUALIFY IF LESS THAN 2YEARS)

4. Please indicate what percentage of time you spend in each of the following areas:
   (Sum must equal 100%)
   IF SUM IS GREATER THAN 100, SHOW WARNING MESSAGE, "Sum must equal 100%."

Type of practice	**Percentage of time spent**
Inpatient care	
Outpatient care	FOR PCPs - DISQUALIFY IF LESS THAN 50% FOR PSYCHs - DISQUALIFY IF LESS THAN 25%
Administration	
Research / Teaching	
SUM (Must total 100%)	(DISPLAY SUM – MUST TOTAL 100%)

For the purposes of this study '*mental health disorders*' will include, but not be limited to, indications such as schizophrenia, bipolar disorder, Attention Deficit Disorder (ADD)/ Attention Deficit Hyperactivity Disorder (ADHD), autism, tourette's syndrome, dementia, delirium, conduct disorders, behavioral disorders, depression, borderline personality disorder, anorexia, psychosis, pervasive developmental disorder, etc.

DISPLAY QUESTIONS 5 TO 7 ON THE SAME SCREEN

5. Approximately, how many patients do you see in outpatient care in a typical week? _____

DISPLAY Q6 TO PCPs ONLY.

6. Of the patients you see in a typical week, how many patients are you treating for any mental health disorders?

   ____

7. DISPLAY Q7a to PCPs ONLY. DISPLAY Q7b to PSYCHs ONLY.

   7a.What percentages of the patients that you treat for mental health disorders would you estimate are in each of the following age groups? Sum of all percentages must equal 100%.

5 years and under	____%
6 to 12 years	____%
13 to 17 years	____%
18 years and older	____% (DISQUALIFY IF 100%)
Total (must sum to 100%)	_____% (DISPLAY SUM)

   IF SUM IS GREATER THAN 100, SHOW WARNING MESSAGE, "Sum must equal 100%."

   7b.What percentages of the patients you see in outpatient care would you estimate are in each of the following age groups? Sum of all percentages must equal 100%.

5 years and under	____%
6 to 12 years	____%
13 to 17 years	____%
18 years and older	____% (DISQUALIFY IF 100%)
Total (must sum to 100%)	_____% (DISPLAY SUM)

   IF SUM IS GREATER THAN 100, SHOW WARNING MESSAGE, "Sum must equal 100%."

8. What percentage of your patients <u>less than 18 years of age</u> that you are treating for mental health illnesses would you estimate have each of the following diagnoses?

   (1) Psychosis - __% (DISQUALIFY IF 0%)

   (2) Bipolar disorder - __%

   (3) Conduct disorder - __%

   (4) Autism - __%

   Total does not have to sum to 100%.

9. What percentage of your patients, less than 18 years of age, is currently in foster care? ___%

10. What percentage of your patients less than 18 years of age that you are treating for mental health disorders are currently taking atypical antipsychotics? ___% (DISQUALIFY IF 0%)

FOR RESPONDENTS WHO DO NOT QUALIFY, SHOW THE MESSAGE BELOW AND TERMINATE:

Thank you for your interest; however, either your profile does not meet our study's needs for this particular study, or we have already filled our quota of respondents who match your profile. We still value your opinion and will contact you in the future with opportunities to complete another study.

FOR RESPONDENTS WHO QUALIFY, SHOW THE FOLLOWING MESSAGE:

Doctor, you meet the criteria for inclusion in our study. The focus of this study is to understand the treatment of mental health disorders in children less than 18 years of age. The remainder of this study will deal with the issues in this treatment area.

11. PATIENT SIMULATION:

- EACH RESPONDENT WILL BE RANDOMLY ASSIGNED TO 1 OF 3 PATIENT PROFILE SETS.
- EACH PROFILE SET SHOULD BE USED THE SAME NUMBER OF TIMES WITHIN EACH SPECIALTY TYPE.
- RESPONDENTS WILL BE SHOWN THE 10 PATIENT PROFILES IN THE ASSIGNED SET.
- THE LAYOUT FOR PATIENT ATTRIBUTE TEXT FIELDS IS GIVEN BELOW. SAMPLE PATIENT PROFILE INCLUDED SEPARATELY.

On the following screens, you will be presented 10 patients whom you might see in your practice. Patients will be presented one at a time. At the bottom of each patient profile screen, you will be asked to indicate your treatment choice for the patient at this time. Please read each patient's information carefully and select all of the treatment options you would use with the patient at this time.

For each patient please assume the following:

- The required work up to support the diagnosis has been completed.
- The patient has insurance coverage that will cover all of the treatment options listed.
- Prior authorization will be required for any antipsychotic prescribed for these patients.

PRESENT 10 PATIENT PROFILES AND RECORD PT_ID AND ALL TREATMENT RESPONSES

PT_NAME

INTRO1 INTRO2

Demographics	Lab values	Symptoms
X1 X2 X3 X4 X5 X6 X7	X8 X9 X10	X11 • X12 • X13 • X14

S1 S2 S3
S4

- S5
- S6
- S7

Treatment options: (Please check all that apply)

Atypical Antipsychotics

☐ Aripiprazole (Abilify®)
☐ Asenapine (Saphiris®)
☐ Clozapine (Clozaril®, generic)
☐ Iloperidone (Fanapt®)
☐ Lurasidone (Latuda®)
☐ Olanzapine (Zyprexa®, Zyprexa Relprevv®, generic)
☐ Olanzapine & Fluoxetine (Symbyax®, generic)
☐ Paliperidone (Invega®, Invega Sustena®)
☐ Quetiapine (Seroquel®, Seroquel XR®, generic)
☐ Risperidone (Risperidal, Risperidal Consta®, generic)
☐ Ziprasidone (Geodon®, generic)

Conventional Antipsychotics

☐ Perphenazine (Trilafon®, generic)
☐ Chlorpromazine (generic)
☐ Others

Anti-convulsants

☐ Lithium (Lithobid®, generic)
☐ Alpha agonists
☐ Other

☐ **Anti-depressants**

☐ **Anxiolytics**

☐ **Mood stabilizers**

☐ **Stimulants**

☐ **Other (Please specify _____)**

☐ **Psychosocial Intervention**

☐ **Refer to another physician with experience in dealing with pediatric mental health**

☐ **Refer to non-medical practitioner**

☐ **Other non-pharmaceutical treatment**

FOLLOW UP:

12. For each of the atypical antipsychotics listed below, please indicate the **level of evidence supporting use** in treating **PSYCHOSIS** within each of the following age groups:
    For purposes of this question:
    'Labeled indication' means that the use of the given drug in the given age group for psychosis is an FDA-approved indication.
    'Medically accepted use but not a labeled indication' means that the use of the given drug in the given age group for psychosis is not an FDA-approved indication, but there is considerable evidence supporting its use.
    'No evidence supporting use' means that the use of the given drug in the given age group for psychosis is not supported by any evidence.
    If you are not familiar with a drug's indications, you can pick *'Don't Know.'*

Product	**Age (years)**	**1 Labeled indication**	**2 Medically accepted use but not a labeled indication**	**3 No evidence supporting use**	**4 Don't Know**
Aripiprazole (Abilify®)	5 & under	☐	☐	☐	☐
	6 – 12	☐	☐	☐	☐
	13 - 17	☐	☐	☐	☐
Asenapine (Saphiris®)	5 & under	☐	☐	☐	☐
	6 – 12	☐	☐	☐	☐
	13 - 17	☐	☐	☐	☐
Clozapine (Clozaril®)	5 & under	☐	☐	☐	☐
	6 – 12	☐	☐	☐	☐
	13 - 17	☐	☐	☐	☐
Iloperidone (Fanapt®)	5 & under	☐	☐	☐	☐
	6 – 12	☐	☐	☐	☐
	13 - 17	☐	☐	☐	☐
Lurasidone (Latuda®)	5 & under	☐	☐	☐	☐
	6 – 12	☐	☐	☐	☐
	13 - 17	☐	☐	☐	☐
Olanzapine (Zyprexa®)	5 & under	☐	☐	☐	☐
	6 – 12	☐	☐	☐	☐
	13 - 17	☐	☐	☐	☐
Olanzapine & Fluoxetine (Symbyax®)	5 & under	☐	☐	☐	☐
	6 – 12	☐	☐	☐	☐
	13 - 17	☐	☐	☐	☐
Paliperidone (Invega®)	5 & under	☐	☐	☐	☐
	6 – 12	☐	☐	☐	☐
	13 - 17	☐	☐	☐	☐

Quetiapine (Seroquel®)	5 & under	☐	☐	☐	☐
	6 – 12	☐	☐	☐	☐
	13 - 17	☐	☐	☐	☐
Risperidone (Risperidal®)	5 & under	☐	☐	☐	☐
	6 – 12	☐	☐	☐	☐
	13 - 17	☐	☐	☐	☐
Ziprasidone (Geodon®)	5 & under	☐	☐	☐	☐
	6 – 12	☐	☐	☐	☐
	13 - 17	☐	☐	☐	☐

13. EVIDENCE BASED PRACTICE ATTITUDE SCALE:

The following questions ask about your feelings about using new types of therapy, interventions, or treatments.

Manualized therapy, treatment, or *intervention* refers to any intervention that has specific guidelines and/or components that are outlined in a manual and/or that are to be followed in a structured or predetermined way. Indicate the extent to which you agree with each item using the following scale:

Statement	**0 Not at all**	**1 To a slight extent**	**2 To a moderate extent**	**3 To a great extent**	**4 To a very great extent**
I like to use new types of therapy/interventions to help my clients.	☐	☐	☐	☐	☐
I am willing to try new types of therapy/interventions even if I have to follow a treatment manual	☐	☐	☐	☐	☐
I know better than academic researchers how to care for my clients.	☐	☐	☐	☐	☐
I am willing to use new and different types of therapy/interventions developed by researchers.	☐	☐	☐	☐	☐
Research based treatments/interventions are not clinically useful.	☐	☐	☐	☐	☐
Clinical experience is more important than using manualized therapy/interventions	☐	☐	☐	☐	☐

I would not use manualized therapy/interventions.	☐	☐	☐	☐	☐
I would try a new therapy/intervention even if it were very different from what I am used to doing	☐	☐	☐	☐	☐

14. For the following statements:

If you received training in a therapy or intervention that was new to you, how likely would you be to adopt it if:

Statement	0 Not at all	1 To a slight extent	2 To a moderate extent	3 To a great extent	4 To a very great extent
it was intuitively appealing?	☐	☐	☐	☐	☐
it "made sense" to you?	☐	☐	☐	☐	☐
it was required by your supervisor?	☐	☐	☐	☐	☐
it was required by your agency?	☐	☐	☐	☐	☐
it was required by your state?	☐	☐	☐	☐	☐
it was being used by colleagues who were happy with it?	☐	☐	☐	☐	☐
you felt you had enough training to use it correctly?	☐	☐	☐	☐	☐

15. Now please think about the decisions you have to make when selecting treatments for patients with psychosis. For each of the following treatment attributes, please rate how well you think each of the listed products performs.

Please rate each product on each attribute using a **7-point** scale where **1 = "Performs poorly on the attribute" and 7 = "Performs very well on the attribute."** If you are not familiar enough with a product to rate it on a goal, please enter a "0"

For most respondents, it is easier to do the ratings across each row.

ROTATE/RANDOMIZE PRESENTATION ORDER OF PRODUCTS AND ATTRIBUTES

	Abilify (aripiprazole)	**Geodon (ziprasidone)**	**Risperdal (risperidone)**	**Seroquel/Seroquel XR (quetiapine)**	**Zyprexa (olanzapine)**
a. Efficacy – Positive Symptoms					
b. Efficacy – Negative Symptoms					
c. Efficacy –Risk of suicide					
d. Dosing/titration					
e. Side Effect – Cognitive Impairment					
f. Side Effect – Metabolic syndrome					
g. Side Effect – QT prolongation					
h. Side Effect – Sexual side effects					
i. Side Effect – Weight Gain					
j. Side Effect- Extra Pyramidal Symptoms					
k. Cost to patient					

PHYSICIAN BACKGROUND: Please answer the following questions about yourself.

16. What is your age? _____

17. What is your gender?
    (1) Male
    (2) Female

18. Which race or ethnicity do you *most* identify?
    (1) White (non-Hispanic)
    (2) Black or African American (non-Hispanic)
    (3) Hispanic or Latino/a (Black or White)
    (4) American Indian or Alaska Native
    (5) Asian American
    (6) Native Hawaiian or Other Pacific Islander
    (7) Other

APPENDIX C: CURRICULUM VITAE

CURRICULUM VITAE
Sujith Ramachandran

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University of Mississippi School of Pharmacy
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EDUCATIONAL QUALIFICATIONS:

- Currently pursuing a **Doctor of Philosophy** in Pharmaceutical Marketing at the University of Mississippi, Oxford, MS. (2011 – present. Expected completion: 2016)
- **Bachelor of Pharmacy** (2007 – 2011) at Osmania University, Hyderabad, India.

EXPERIENCE:

- **Marketing Intern**, *Bavarian Nordic Immunotherapeutics*, Mountain View, CA (June – August 2013): Responsibilities include:
  - Competitive landscape analysis and market overview
  - Physician participation in prostate cancer clinical trials: A primary research study assessing motivators, barriers, contact strategies, product ratings and perceptions of clinical trials in advanced prostate cancer
  - Health economic and market analogue analysis
- **Research assistant**, Center for Pharmaceutical Marketing and Management, University of Mississippi. (January 2013 – June 2013)
  - **Mississippi Division of Medicaid, Drug Utilization Review** team: Analysis of Mississippi Medicaid fee-for-service data using SAS®
- **Research Assistant,** Department of Pharmacy Administration, University of Mississippi. (August 2011 – July 2012)
  - **Delta Health Patient Care Management Project, funded by the Delta Health Alliance (DHA) - HRSA Grant Number U1FRH07411-3:** Data entry, management and analysis for the years 2009 – 2012 using Microsoft Excel and SPSS®.

RESEARCH SKILLS:

- Survey design, data entry, data collection, management & analysis.
- Advanced user/programmer in Microsoft Excel®, SPSS® and SAS®.

- Focus group discussion guide design and moderation.
- Development of online – surveys using Qualtrics™.
- Proficiency in using secondary data including data management and analysis.
- Model development and analysis using TreeAge® Pro suite.

RESEARCH:

- **Ramachandran S,** Banahan BF, Bentley, JB, West DW, Patel A. Determining the physician and product factors influencing the use of atypical antipsychotics in children. Presented at *Pharmaceutical Marketing Research* Group conference, Jersey City, NJ, October 2013.
- **Ramachandran S**, Null KD. Identifying high cost patients in managed care: An application of fractal mathematics. *Association of Managed Care Pharmacy* conference, San Diego, CA, October 2013.
- **Ramachandran S**, Mahabaleshwarkar R, Yang Y. Cost effectiveness analysis of addition of telaprevir or boceprevir to standard therapy versus standard therapy alone for the treatment of previously untreated chronic hepatitis-C virus genotype 1 infection. *International Society of Pharmacoeconomics and Outcomes Research*, Washington DC, June 2012.
- **Ramachandran S**, Mahabaleshwarkar R, Yang Y. Cost consequence analysis of telaprevir versus boceprevir for the treatment of previously untreated chronic hepatitis-C virus infection. *Meeting in the Middle*, Austin, TX, June 2012.
- 'Medication Adherence Intervention - environmental scan and literature review.' Research Grant proposal. Funded by **National Community Pharmacists' Association (NCPA)** - $5000.
- 'Optimization of Outcomes and Revenues of Pharmacist-provided Medication Therapy Management Services.' Departmental best research grant proposal submitted to the **Community Pharmacy Foundation (CPF).**
- 'What, if anything, has changed in the last twenty years? An examination of stress in school of pharmacy faculty.' A national survey of Pharmacy school faculty and a focus group conducted using faculty from the University Of Mississippi School Of Pharmacy. Presented at the *American Association of Colleges of Pharmacy Conference*, Chicago, IL, July 2013.
- 'Health care expenditure associated with off-label use of atypical antipsychotics in Medicaid children.' A retrospective analysis of Mississippi Medicaid data. Presented at the *International Society of Pharmacoeconomics and Outcomes Research conference*, New Orleans, June 2013.
- Khanna, R., Jariwala, K., Holmes, E. R., & **Ramachandran, S**. (2013). Autism Familiarity and Knowledge among Pharmacy Students. *Currents in Pharmacy Teaching and Learning*.

PROFESSIONAL CITIZENSHIP:

- Rho Chi Academic honors society, 2013 initiate.
- Phi Kappa Phi academic honors society, 2013 initiate.
- Secretary for the International Society of Pharmacoeconomics and Outcomes Research (ISPOR) student chapter, 2012-13.
- Vice-President of the University of Mississippi Graduate Student Council, 2013 – 2014.

- Vice-President of the UM Pharmaceutical Marketing Research Group student chapter, 2013 – 2014.
- Senator for the department of Pharmacy Administration in the University of Mississippi Graduate Student Council, 2012-13.