SAFETY AND APPROPRIATENESS OF ANTIPSYCHOTIC MEDICATIONS FOR MEDICAID CHILDREN UNDER AGE 16

Report to the Texas Legislature

As Required by
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Texas Health and Human Services Commission

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Executive Summary

H.B. 2163, 81st Legislature, Regular Session, 2009, requires that the Texas Health and Human Services Commission (HHSC) conduct a study and submit a report by November 10, 2010, on the appropriateness and safety of providing antipsychotic medication through the Medicaid Vendor Drug Program to children younger than 16 years of age. This legislation was based on concerns regarding the increased use of these medications in Medicaid children during the past decade. Questions arose whether these medications are safe for children and whether prescribing them to children, particularly off label (without an approved indication by the United States Food and Drug Administration [FDA]), is appropriate.

This report provides a descriptive review of the current situation as documented in professional research literature and state, federal, and national public information. It relies on existing data and analyses. The literature review included more than 200 references published between 2000 and 2010.

Report Scope of Work

In order to determine whether it is safe to provide antipsychotic medications to children in Medicaid younger than 16 years of age, the report reviews the following information regarding the safety of these medications, particularly for children younger than 16 years of age:

- Identify FDA-approved indications and age ranges for each antipsychotic drug
- Describe the use of off-label prescribing with patients of all ages and medical needs.
- Ten-year literature review of child and adolescent medication studies, noting the source of funding where possible.

In order to determine whether it is appropriate to provide antipsychotic medications to children in Medicaid younger than 16 years of age, the report evaluates the following issues from FDA information, the ten-year literature review, and clinical practice:

- Efficacy of antipsychotic medications
- Consistency of use with the standard of care
- Informed consent
- Side effect profiles
- Access to quality medical care

Antipsychotic medications include typical (first generation) and atypical (second generation) medications, both of which are reviewed in this report. There has been more research on antipsychotics in youth in the last ten years than occurred in all the previous years combined. The report reflects that the overwhelming majority of the research in the past ten years addresses the newer second generation antipsychotics (SGAs), with the older first generation antipsychotics (FGAs) only appearing in comparison studies.

Summary of Findings on Appropriateness and Safety

Below is a summary of the report's findings. Additional details on these findings are in the body of the report.

FDA approved indications for youth and the scientific evidence reflected in the literature review (Tables A-I) both document short and intermediate term safety and efficacy of many antipsychotic medications in a number of pediatric behavioral health conditions, including schizophrenia, bipolar disorder, autism, tic disorders, and aggression. Treatment guidelines for most of these disorders generally recommend using antipsychotic medications after psychosocial interventions have been shown to be insufficiently effective, though they may be used as primary treatment for schizophrenia and bipolar disorder. In practice, however, medication sometimes is used as first-line treatment for other diagnoses as well, particularly if it is difficult to access psychosocial interventions and/or if there is a need to stabilize a patient quickly.

Appropriate assessment leading to accurate diagnosis is key in determining an appropriate choice of treatment. The choice of when to use an antipsychotic depends on the diagnosis, severity of the symptoms, risk to the youth and others of not using an antipsychotic, availability of other effective evidence-based treatments, and the resources of the community and family to support treatment.

Based on the legal measure of "standard of care," antipsychotics have been used in youth for a long time and physicians are trained and expected to use them for certain indications in children and adolescents by their professional colleagues. Based on each child's needs, the clinician, together with the responsible adult(s) and patient, must weigh the risks and benefits of any given treatment, including prescription medication. Parents and guardians must consent to treatment for their children, and should receive complete, high quality information to enable them to make treatment decisions.

Off-label prescribing is the norm in all pediatric care, with a recent study showing that approximately 62 percent of all pediatric prescriptions are prescribed off label.[1] This is an artifact of the historical FDA drug approval process. It does not occur at higher rates in pediatric psychiatric care than in general pediatrics.

The literature shows that the antipsychotics have efficacy in the same disorders in youth as they do in adults with one exception—they have not shown efficacy in youth depression. The literature also describes the same side effects and adverse effects as in adults, although probably at higher rates. If selected properly after careful assessment, and with ongoing screening for adverse effects, the literature confirms that antipsychotic use appears safe in select preschool, school age, and older children for treatment for up to three years in duration.

There are, however, several areas in which there is little to no high quality evidence on the use of antipsychotics:

- The use of multiple concurrent antipsychotic medications in youth.
- The use of any antipsychotic in children under 3 years of age (with only minimal evidence for use in those 3 to 5 years old).
- The long-term effects (greater than three years) of any of the antipsychotics.

Obesity is the biggest concern with second generation antipsychotics, with an attendant risk of metabolic syndrome, and later, heart disease and diabetes. Neuromuscular effects (e.g. involuntary movements, extreme restlessness) are the biggest concern with the first generation antipsychotics. Parents and practitioners must make decisions about the trade off between these two types of adverse effects when choosing antipsychotic medications. Careful management of patients can ameliorate the risks attendant to both types, but it is difficult to make lifestyle changes related to diet and exercise and Medicaid youth often do not access periodic services such as lab tests required to monitor for adverse effects.

HHSC solicited stakeholder input on a draft version of this report and received 20 responses, some generally supportive of the report and others critical of various aspects of the report. The full text of those responses is included as Appendix I, which also notes which comments were used to modify the report from the draft version to this final version.

Options for Texas Medicaid

The Texas Health and Human Services agencies have already taken steps to encourage the appropriate prescribing of antipsychotic medications, particularly among children in foster care who are known to be prescribed these medications at a significantly higher rate than other children in Medicaid. A newly released study of 16 states highlighted 36 practices that states have undertaken to encourage appropriate prescribing of antipsychotic medications for children and adolescents (See Appendices C and H). While the study was not released in time for HHSC's analysis of the 36 practices included, one of the practices noted as a promising practice is Texas' *Psychotropic Medication Utilization Parameters for Foster Children* (Texas Parameters). These parameters were initially released in February 2005 and have been periodically updated to guide utilization review of psychoactive medications for the foster care population, including the use of antipsychotics, antidepressants, stimulants and mood stabilizers (See Appendix A). The other 16 states' practices vary and range from policy development and implementation, stakeholder engagement, education/marketing, patient-provider feedback, to system interventions.

The Conclusions and Options section of this report, which appears before the other sections for ease of access, lists various options policymakers may want to consider to further encourage the appropriate prescribing of antipsychotic medications to children in Medicaid. Some of these build on the Texas Parameters and their successful use in the foster care population. As with all decisions related to Medicaid coverage, it is important to balance access to care with ensuring the safety and quality of care.

I - Conclusions and Options for Texas Medicaid

For ease of access, this section appears before the remainder of the report. The discussion and references to support the conclusions listed here are located within Sections II – VII.

What We Know

- Evidence-based assessment leading to accurate diagnosis is key in determining an appropriate choice of treatment.

- Antipsychotic medications have legitimate therapeutic uses in children and adolescents for schizophrenia, bipolar disorder, autism, tic disorders, and aggression.

- Antipsychotic medications are generally well tolerated in the clinical studies available, where benefits appear to outweigh risks.

- Obesity is the biggest concern with the second generation antipsychotics and neuromuscular effects are the biggest concern with the first generation antipsychotics. Careful management of patients can ameliorate the risks attendant to both types.

- There is little to no high quality evidence on the use of multiple concurrent antipsychotic medications in youth.

- There is little to no high quality evidence on the use of any antipsychotic in children under 3 years of age and only minimal evidence for those 3 to 5 years old.

- There is little to no high quality evidence on the long-term effects (greater than 3 years) for any of the antipsychotics and no effective national or local system in place to gather this data.

- The second generation antipsychotics have a fairly large and growing high quality clinical trial evidence base. The first generation antipsychotics do not, as they have been only evaluated via comparison studies during the ten-year review period.

- At least 31 of the 95 studies that met the review criteria for this report were funded by a governmental or nonprofit entity, with 6 of these receiving some financial support from the pharmaceutical industry and some others receiving donated medications. The remaining studies were either funded by the pharmaceutical industry or did not list a funding source.

- Risperidone has the largest clinical trial evidence base of all the antipsychotics in the under age 18 population.

- In a 2004-2007 study, Texas Medicaid youth as a whole were being treated with antipsychotic medications at rates below the average of 16 other studied states, but the rate is rising.

- From 2004 through 2007, Texas Medicaid youth in foster care were being treated with antipsychotic medications at rates higher than the average of 16 other studied states.

- From 2004 through 2007, Texas Medicaid children under 6 years old were being treated with antipsychotic medications at rates higher than the average of 16 other studied states.

- Overall rates of antipsychotic use in Texas Medicaid youth are increasing, while rates in the foster care population are decreasing.

- From 2004 through 2007, utilization rates of multiple concurrent antipsychotic medications decreased in both the general Medicaid youth population and children in foster care.

- From 2004 through 2007, utilization rates of antipsychotic medications for children under age 6 decreased in both the general Medicaid children's population and among children in foster care.

- These drops likely are related to the wide distribution and application of the *Texas Psychotropic Medication Utilization Parameters for Foster Children* (Texas Parameters) initially released in 2005.

- Off-label prescribing is the norm in all pediatric care. This is an artifact of the historic FDA drug approval process. It does not occur at higher rates in pediatric psychiatric care than in general pediatrics.

- Treatment guidelines for most pediatric psychiatric disorders generally recommend using antipsychotic medications after psychosocial interventions have been shown to be insufficiently effective, though they may be used as primary treatment for schizophrenia and bipolar disorder.

- When given complete, high quality information, parents and guardians are in the best position to make treatment decisions about the youth in their care—including decisions about off-label medication use.

Options to Consider

Below are some options to consider for encouraging the appropriate prescribing of antipsychotic medications to Medicaid recipients under age 16. Some of these considerations build on the Texas Parameters and their successful use in the foster care

population. HHSC is moving forward with initiatives related to two of these options (2 and 7).

As with all decisions related to Medicaid coverage, it is important to balance access to care with the safety and quality of that care. Also, in a challenging fiscal environment, please note that while HHSC has not estimated the cost of each of these options, some may require significant additional resources.

1. Formally extend the Texas Parameters used for children in foster care to the overall Medicaid youth population in all service delivery models. Inform Medicaid prescribers that HHSC may use the Texas Parameters as a quality evaluation tool for record review for the overall Medicaid youth population.

2. Provide additional educational information to all Medicaid providers who treat children and adolescents and particularly to Medicaid providers who prescribe antipsychotic medications to a large number of Medicaid children as well as to those who most frequently prescribe outside of the Texas Parameters (e.g. prescribing two or more antipsychotics concurrently or prescribing them to very young children). Education also could include information on the importance of certain tests for monitoring for adverse effects in children prescribed antipsychotics (e.g. glucose testing, lipid screening), the elements of informed consent, and levels of evidence for off-label prescribing.

   In August 2010, the Texas Medicaid Drug Utilization (DUR) Review Board, an advisory body comprised of physicians and pharmacists, requested that HHSC develop a retrospective intervention letter to targeted Medicaid prescribers on the use of atypical antipsychotics in children and the issues related to obesity and metabolic disorder with the use of these drugs. HHSC will develop a proposed letter to present to the DUR Board at its next meeting.

3. Consider extending the utilization review process of antipsychotic medications currently in place for the STAR Health population of children in foster care to the overall Medicaid youth population.

4. Specifically, extend the STAR Health class polypharmacy utilization review process for two or more antipsychotic medications prescribed concurrently to the overall Medicaid youth population.

5. Facilitate consultation, including via telemedicine, for non-psychiatrists serving Medicaid youth with mental health disorders, particularly in areas of the state where there are psychiatrist shortages.

6. Consider options to provide additional psychosocial services to Medicaid children. For example, add as a Medicaid benefit the procedure codes for integrated health care. This would extend statewide an HHSC pilot project that integrates licensed

mental health practitioners into pediatric primary care practices to provide preventive behavioral health services and facilitate referrals to a child psychiatrist as needed.

7. Review the availability (or lack thereof) of intensive behavioral interventions for the Medicaid population and restrictions on inpatient length of stay, which may encourage increased antipsychotic use due to the need to stabilize a child quickly.

8. Review the 36 practices contained in the June 2010 report titled "Antipsychotic Medication Use in Medicaid Children and Adolescents: Report and Resource Guide from a 16-State Study" for their applicability to the Texas Medicaid program. The report was not released in time for analysis of the 36 practices to be included in this report, but is included as Appendix H.

9. Consider basing any prior authorization for antipsychotics on the "Criteria Indicating Need for Further Review of a Child's Clinical Status" in the Texas Parameters (e.g. multiple antipsychotics prescribed concurrently, use in very young children). It would be appropriate for the DUR Board to advise HHSC on the establishment of any prior authorization criteria.

   Based on the information in this report, HHSC is in the process of putting two new Vendor Drug Program prior authorization requirements in place – for any antipsychotic prescription to a Medicaid child under age 3 and for the third antipsychotic medication prescribed concurrently to any Medicaid recipient under age 18. The DUR Board will provide input on these prior authorization criteria and HHSC will need to modify the pharmacy claims system to implement them.

10. Provide information to help guide parents' and patients' decision-making as it relates to off-label prescribing of antipsychotic medications. This information should include all the elements necessary for a formal consent process, including the potential side effects related to these medications and the importance of diet, exercise, and follow-up appointments to monitor for adverse effects.

11. Consider institution of an adverse event reporting system through the STAR Health electronic health passport for children in foster care. The population is large enough to provide statistically valid information and the system is already in place so costs are minimized. Also, with the Department of Family and Protective Services (DFPS) as conservator, privacy concerns over starting a new database are minimized.

12. Consider funding a true research-style analytical study that will inform policy and provide methodology for developing statistically valid ongoing reports into the future. Potential study areas include the use of antipsychotics for the treatment of aggression and the mapping of diagnoses to antipsychotic use for various Medicaid youth subpopulations (such as youth in foster care, youth being served by mental health system, and the remaining Medicaid youth population). Another potential study area would be a long term outcome study to assess the health impact of the Texas Parameters on youth in foster care.

II - Introduction

Legislative Background

H.B. 2163, 81st Legislature, Regular Session, 2009, requires that the Texas Health and Human Services Commission (HHSC) conduct a study and submit a report by November 1, 2010, on the appropriateness and safety of providing antipsychotic or neuroleptic medication through the Medicaid Vendor Drug Program to children younger than 16 years of age.

The study must consider the following factors relevant to the appropriateness and safety of providing the medications to children:

1. the physical and psychological medical diagnosis of a child's condition;
2. whether the U.S. Food and Drug Administration (FDA) has approved a medication for use by a child of a certain age;
3. whether a child has successfully taken a medication previously;
4. access to quality medical care for a child receiving benefits under the program;
5. the standard of care in the medical profession regarding the provision of such medications to a child; and
6. any other factor HHSC considers relevant.

While H.B. 2163 refers to "antipsychotic or neuroleptic" medications, these terms represent a single class of medications. For the purposes of this report, these medications will be referred to as antipsychotics. Antipsychotic medications include typical (first generation) and atypical (second generation) medications, both of which are reviewed in this report.

Context

HHSC was charged with providing this report due to concerns among certain members of the public and elected officials about inappropriate prescribing of antipsychotic medications to Medicaid children younger than age 16. There are concerns that these drugs are unsafe for children, and that they often are prescribed off-label (without approval by the FDA for use in children for certain diagnoses). The goal of the Medicaid program and its providers is to keep Medicaid children safe and provide them appropriate care.

Several factors bring the use of antipsychotic medication in children and adolescents into the public eye. First, the practice of psychiatry has been transformed in recent years by research into the brain that has highlighted the biological aspects of psychiatric disease. Physician training now emphasizes the use of medications for behavioral disorders, sometimes at the expense of training in psychosocial interventions. Psychiatric medicine, which had long lagged behind the rest of medicine in its ability to provide quick relief

based upon an understanding of causation of disease, appeared to be catching up. Money flowed into researching biological treatments.

Second, this emphasis on biological psychiatry has come at a time when many new antipsychotics, the second generation, have come on the market. Prior to the recent era, the first generation antipsychotics (FGAs) were perceived to have many undesirable neurological effects. They could cause stiff or cramped muscles, unwanted muscle movements, and sometimes a syndrome of dysfunctional muscle movements that did not go away when the medications were discontinued. Many of the oldest medicines in this class commonly caused blurry vision, dry mouth, and difficulty urinating—unpleasant side effects that although not dangerous, certainly were perceived by patients as unpleasant. Then a breakthrough occurred.

In 1989, clozapine was introduced to the U.S. market. This medication was able to treat patients who had never before responded to any antipsychotic medication, and had virtually no neurological side effects. Unfortunately, because of its tendency to cause a potentially fatal blood disorder, it was not a first line treatment. Pharmaceutical companies raced to find medications that had the positive characteristics of clozapine without the risk of serious adverse effects. The race produced many other second generation antipsychotics (SGAs). At first, the perceived significant decreased frequency of neurological side effects led physicians to prescribe these medications more freely than they had in the past—including prescribing them more often for children and adolescents. Many patients tolerated them better than the old drugs because of differing side effects that may not have caused immediate discomfort.

Third, we now know that there are significant adverse effects for the SGAs that were not completely understood when they were first introduced. Increased appetite with resultant weight gain caused by these medications increases the risk of metabolic syndrome—a condition that can lead to diabetes, heart disease, and hypertension. The elucidation of metabolic syndrome and its relationship to these long term risks is an evolving area of medicine that has undergone its own transformation as the American population as a whole has become increasingly obese. Children and adolescents are generally thought to be more susceptible to the adverse effects of both the FGAs and the SGAs, including the propensity to gain weight. Still, the SGA medications were reported to be better tolerated by patients than the old ones had been.

Fourth, more youth are being referred and treated for behavioral health problems. This has occurred for a number of reasons. The increasing incidence of disorders in the autism spectrum such as Asperger's syndrome as well as the recognition that children may suffer from bipolar disease have brought more youth into treatment for psychiatric problems. Increased visibility of mental disorders in the mainstream media has led to more recognition of these problems. The President's New Freedom Commission on Mental Health in 2002 increased recognition, referral, and treatment of mental disorders. Teachers have been trained and encouraged to recognize and quickly refer students with potential mental health problems. Funding for psychiatric treatment has increased due to the efforts of advocacy groups seeking parity with funding for treatment of other

disorders. The proportion of the youth population eligible for public health benefits has also increased due to new programs such as the Children's Health Insurance Program (CHIP) and growing Medicaid enrollment. As more children and adolescents have been referred to treatment, more have been exposed to antipsychotic treatment. The use of the SGAs has become more visible to more people.

Fifth, the proportion of public and privately funded health care budgets spent on psychiatric medications has become quite significant. In state fiscal year 2009, Texas Medicaid spent almost $72 million on antipsychotic medications for children and adolescents under age 16. In an era of economic difficulty, cost containment of health care expenditures at all levels has become increasingly important. The use of psychiatric drugs in general and their use in youth in particular has come under increasing scrutiny by governments seeking to cut budgets and reduce taxes.

Sixth, due to fear, lack of understanding, and the stigma of mental illness, issues relating to psychiatric care have historically attracted and still attract more scrutiny and negative attention than other areas of medical care. A significant proportion of people still consciously and unconsciously practices discrimination in this area.

These six factors have led to increasing public debate on the use of antipsychotics in children and adolescents.

Texas Enters the Debate

Texas entered the nascent public debate caused by the confluence of the above six factors in 2004 when the HHSC Office of Inspector General (OIG) released a report that raised concerns about the use of psychotropic medications by children in Department of Family and Protective Services (DFPS) conservatorship. The report used financial claims data to question the number of children on these medications, the young age of children being treated, and the use of multiple concurrent medications.

In response to these concerns, DFPS and HHSC convened an advisory panel and with the help of the Department of State Health Services (DSHS) in February 2005 released the initial *Psychotropic Medication Utilization Parameters for Texas Foster Children* (Texas Parameters). These prescribing guidelines provide parameters for the appropriate use of psychotropic medications (including antipsychotics, antidepressants, stimulants and mood stabilizers) in children in foster care and also alert clinicians to situations that indicate a need for further review of a patient's case. HHSC, DFPS and DSHS periodically update the parameters to reflect the most current clinical information on these medications (See Appendix A).

In 2006, HHSC, DFPS, and DSHS released a new analysis of claims data for the foster care population based upon criteria in the Texas Parameters. The analysis focused on four of the criteria outlined in the guidelines:

- Absence of a mental health diagnosis
- Five (5) or more psychotropic medications prescribed concurrently

- Prescribing two or more medications from the same drug class concurrently
- Prescribing psychotropic medication for very young children

This report, which addressed methodological flaws in the OIG report, accounted for the way clinical medicine is actually practiced, how it plays out in patient behavior, and the limited clinical information contained in claims data used to pay providers. For example, many of the medications used for psychiatric conditions also are used in neurology, and pharmacy prescription claims do not contain diagnoses that would allow an analyst to determine the reason the medication was prescribed. The HHSC 2006 report addressed many other similar difficulties in using claims data to come to conclusions about clinical matters.

The picture that emerged from HHSC's analysis confirmed that levels of prescribing to youth in foster care were high, but not to the degree shown in the 2004 report. It also provided a methodology to continue to track prescribing behavior that formed the basis for drug utilization review going forward.

As a result of this report and other health care issues in this population, HHSC and DFPS instituted training for providers, care managers, and judges, and in April 2008, implemented STAR Health, a managed health care system for Medicaid youth in foster care. The STAR Health managed care system includes a medical home model, electronic health passport, and a utilization review system based on the Texas Parameters to monitor clinical psychiatric prescribing.

Since 2005 and likely as a consequence of these changes, physicians have prescribed fewer psychoactive medications in this population. From 2004 to 2009, the percentage of youth in foster care receiving a psychoactive medication for 60 or more days decreased by more than a third from 29.9 percent to 19.7 percent. HHSC's analysis of psychoactive medication prescribing to youth in foster care is updated yearly and placed on the HHSC website. (See Appendix B)

Seven patient profiles from the STAR Health psychotropic medication utilization review process are imbedded throughout this report to provide real-life examples of Medicaid children in foster care who received antipsychotic medications. These scenarios do not reflect the non-pharmacologic treatment interventions that each child received, but rather illustrate the types of situations in which children and youth of various ages are prescribed antipsychotic medications.

The HHSC 2006 report on children in foster care also played a part in the Antipsychotic Prescribing (AP) in youth project undertaken by the Medicaid Medical Directors Learning Network and the Agency for Healthcare Research and Quality (AHRQ)-funded Rutgers Center for Education and Research on Mental Health Therapeutics (CERT). The methodology used in Texas was refined further, combined with efforts of other states, and used to compare data from these states. This provided a national picture of antipsychotic prescribing in Medicaid youth populations. Results from this effort, which

were released in July 2010, are discussed in Section VI of this report. (See Appendix C for Texas-specific results from the study and Appendix H for the full report.)

When the 81st Legislature met in 2009, the issue of antipsychotic prescribing in Texas rose again in the context of the entire Medicaid youth population. Again claims data excerpts alleged that inappropriate prescribing is occurring on a large scale, especially to the youngest age groups. Proposed legislation would have limited access to these medications by requiring prior authorization for every prescription to Medicaid youth younger than 11 years old. After debate, the Legislature passed H.B. 2163, which requires a report on the safety and appropriateness of prescribing antipsychotic medications to youth under age 16 in the Texas Medicaid program. This report is intended to meet the H.B. 2163 requirements.

III - Texas Medicaid Context

Federal law requires that Medicaid cover a comprehensive set of health care benefits for recipients under age 21. In Texas, these benefits are delivered through one of several managed care models or fee-for-service depending on where the recipient lives and the type of Medicaid coverage the recipient has.

The Texas Medicaid Vendor Drug Program covers most outpatient prescription drugs through contracts with over 4,100 pharmacies. As required by federal law, the Vendor Drug Program maintains a comprehensive formulary of all drugs of manufacturers that have signed a federal Medicaid rebate agreement. Medicaid's formulary includes the following antipsychotic medications, with the generic name shown followed by the most recognizable brand name in parentheses (drugs may be sold under multiple brand names):

- Second Generation Antipsychotics – aripiprazole (Abilify®), clozapine (Clozaril®), olanzapine (Zyprexa®), quetiapine (Seroquel®), risperidone (Risperdal®), ziprasidone (Geodon®), iloperidone (Fanapt®), paliperidone (Invega®), and asenapine (Saphris®)

- First Generation Antipsychotics – chlorpromazine (Thorazine®), haloperidol (Haldol®), molindone (Moban®)* (this medication was withdrawn from the market and no longer available after June 30, 2010), perphenazine (Trilafon®), pimozide (Orap®), thioridazine (Mellaril®), thiothixene (Navane®), fluphenazine (Prolixin®), and trifluoperazine (Stelazine®)

Appendix D contains more detailed information on Texas Medicaid benefits for children, the Medicaid Vendor Drug Program for outpatient prescription drugs, and the Medicaid delivery models that are used throughout the state.

There are physician workforce shortages in many parts of Texas, particularly among specialists and subspecialists. While psychiatrists often treat the children with the greatest behavioral healthcare needs, primary care providers often treat children with behavioral health-care needs and prescribe them psychoactive medications, including

antipsychotic medications. This would be particularly true in counties where there is no psychiatrist. See Appendix E for further details on the shortage of psychiatrists, and particularly child and adolescent psychiatrists, in Texas.

IV - Safety

The first concern in the prescription of antipsychotics for youth is the first precept of medicine, "First do no harm." Safety of medications on the market in the U.S. is under the jurisdiction of the FDA. The FDA's role has evolved and expanded over the years and it is currently instrumental in encouraging the expansion of the evidence base on antipsychotic prescribing in youth. Once on the market, more evidence about short and long-term safety becomes available from clinical trials and adverse event reporting.

FDA Drug Approval

In 1938, Congress passed the Federal Food, Drug, and Cosmetic Act (FFDCA), which mandated that new drugs be shown safe before marketing. The Durham-Humphrey Amendment in 1951 defined the kinds of drugs that cannot be used safely without medical supervision, including limiting access to prescription by a licensed practitioner. Proof of effectiveness was mandated by the Kefauve-Harris Drug Amendments in 1962.[2] This time frame coincides with the introduction of antipsychotic medications in the U.S.

Companies that wish to sell a drug in the U.S. must first test it in animals and then in people. The results of these tests are sent to the FDA where a team of independent experts reviews all the information submitted. Drugs whose benefits are determined to be greater than their known risks are then approved for sale in the U.S. The label for the drug must list only those health conditions and populations for which the company has provided evidence of safety and efficacy.[3]
This process has three main limitations:

1. The pharmaceutical companies that fund the studies will market and financially profit from the drug.
2. The studies are generally short term (weeks to months) in length and therefore may not uncover long-term risks.
3. The FDA is partly funded by fees it receives from pharmaceutical companies.

Additionally, before or after granting marketing approval, FDA may ask the manufacturer to conduct a "phase 4" or "postmarketing" study. This request is made if the FDA concludes that additional information, while not essential for approval, is important in improving the prescribing and use of the product; product quality; or consistency in product manufacturing. Postmarketing studies may confirm existing data, raise or answer questions, or provide new data.[4]

Frequently, pediatric studies are performed on a postmarketing basis. This occurs when the drugs have already been on the market a long time or the drug is being approved for adult health conditions but pediatric studies are still needed. Once on the market, the FDA also accepts new studies from drug companies wishing to add new indications for

marketing approval, and tracks the reporting of adverse events through the voluntary MedWatch system (See below.)

The FDA approval process does not constitute the regulation of the practice of medicine, nor control how medications are used by licensed professionals once they have been approved for marketing. The following explanation is taken from a government report: [5]

> FDA Does Not Regulate Medical Practice
>
> Although drugs are made available under the FFDCA for use in medical practice, the Food and Drug Administration (FDA) has repeatedly determined that neither the FDA nor Congress regulates medical practice "as between the physician and patient" (Federal Register 1972). FDA policy is that good medical practice and patient interest require that physicians be free to use drugs according to their best knowledge and judgment (Federal Register 1975). The Federal courts have supported the principle that FDA does not regulate medical practice (U.S. vs. Evers 1981).
>
> FDA Does Not Restrict 'Off-label' Uses
>
> The foreword to the Physician's Desk Reference recognizes that the FFDCA does not limit the manner in which a physician may use an approved drug. Once a product has been approved under the FFDCA for marketing, a physician may prescribe it (although it may not be advertised or promoted) for uses or in treatment regimens or patient populations that are not included in the approved labeling (Federal Register 1983).
>
> New uses for drugs are often discovered, reported in medical journals and at medical meetings, and subsequently may be widely used by the medical profession.... When physicians go beyond the directions given in the package insert it does not mean they are acting illegally or unethically, and Congress does not intend to empower the FDA to interfere with medical practice by limiting the ability of physicians to prescribe according to their best judgment. (U.S. vs. Evers 1981)[5]

FDA Drug Approval and Youth

Historically about 75 to 80 percent of drugs in the U.S. have had no FDA-approved marketing indications for children and adolescents.[6,7] The FDA states, “By necessity, doctors have routinely given drugs to children "off label"…”[7] There are 3 main reasons for this:

1. There has been no compelling business incentive for pharmaceutical companies to perform safety and efficacy studies for use in children and adolescents. Conducting studies is very expensive. This investment would not result in increased revenue

because once on the market for any indication, the medications may be prescribed for youth anyway.

2. Conducting human research trials with youth has ethical and practical hurdles. Children and adolescents cannot legally give consent to become research participants, but still must agree to participate. Parents are naturally very reluctant to consent to allowing their children to participate in medical research, especially for milder conditions. Research treatment, especially with young children, is inherently more time consuming and inconvenient than regular treatment due to the extra assessment, specially trained clinicians and environments needed, and documentation requirements. It may therefore also incur extra costs to the participants.
3. The best research uses a placebo control, but few parents of child research participants with serious illnesses wish to take the risk of their child receiving no treatment for their disorder by being in the placebo group.

Patient profile from STAR Health psychotropic medication utilization review process

Case #1: 20-month old male with prolonged periods of crying lasting 1-2 hours, inability to soothe himself, and increased agitation with touch, making feeding, bathing, and diaper changes extremely difficult. He cannot be held as this will trigger crying episodes and repeated head banging and biting. He is only sleeping 2-3 hours at night. He can walk but runs away from everyone. He is delayed in his language development and does not use even basic words. By report, mother used multiple drugs during pregnancy. The neurologist has started low dose risperidone to reduce sensory hypersensitivity, head banging, and crying episodes.

Psychological factors in this case are difficult to assess in a child this age, but this child does not appear to be able to bond or interact with others. This further affects his ability to interact with others, and increases the risk of neglect and physical abuse.

Psychiatric/behavioral symptoms that are prominent in this case include severe sensory integration disorder, self-abusive behavior (severe head banging, biting self), prolonged agitation, sustained crying, severe disrupted sleep patterns, and the possibility of pervasive developmental delays/autism.

The use of atypical antipsychotic medication would be off label, but supported by the severity of symptoms.

As noted previously, lack of FDA marketing approval for pediatric indications does not necessarily mean that these drugs do not have efficacy or safety data. It also does not mean that their use is illegal, unprofessional, or unethical. It does mean that the manufacturer has probably not conducted studies and therefore has not sought approval from the FDA for marketing for pediatric uses. Other entities such as universities, private foundations, and even the federal government can and do conduct medication studies in children that may establish safety and efficacy.

To combat the FDA approval situation, Congress passed the Food and Drug Administration Modernization Act (FDAMA) of 1997, which extended the exclusive marketing rights of drug companies by six months if they carried out studies in children. This was augmented in 1998 when the FDA put forth the Pediatric Rule. This regulation, which faced legal challenge, required pharmaceutical companies to conduct safety and efficacy studies in children for select new and old drugs. In 2002, the Best

Pharmaceuticals for Children Act continued and strengthened the FDAMA by clarifying and amending procedures for generic drug approval when pediatric indications are added to labeling. And finally, in 2003, settling the legal problem with the Pediatric Rule, the Best Pharmaceuticals for Children Act gave the FDA the legal authority to require that drug companies conduct clinical studies of pediatric uses for new drugs.[2] These legislative and regulatory changes have resulted in more pediatric drug research in the last 5 years than in the previous 30 years.[7]

In spite of these changes, however, the majority of pediatric prescriptions written in the U.S. today are still for off-label indications. One 2009 study of pediatric outpatient visits estimated that 62 percent of all visits resulted in off-label prescribing. The percentage of prescriptions written for off-label indications varied by the type of medication. About 96 percent of all cardiovascular-kidney, 85 percent of pain, 80 percent of gastrointestinal, and 67 percent of lung and skin medications were prescribed to youth in the absence of FDA-approved marketing indications. Specialists prescribed off label at higher rates than non-specialists and younger children received more off-label prescriptions than older children. (Even when pediatric studies have been done for submission to the FDA, rarely are children younger than age 3 included.) In the 2009 study referenced above, risperidone was the only antipsychotic to make the list of top five central nervous system drugs prescribed off label. It ranked 31st overall behind many antibiotics, lung medications, upper respiratory drugs, and skin preparations.[1]

Safety and Tolerability of Antipsychotic Medications in Youth

Papers describing clinical trials with medications document measures of efficacy and report on adverse events. Adverse events must be distinguished from adverse effects and side effects. An adverse event is any occurrence of an undesirable health episode during a clinical trial or while taking a medication. This event may or may not be relevant to the medication under study or being used. For example, a study participant may be in a car accident during the time of the clinical trial. This is an adverse health event and would be reported in the study; however, it is not related to the medication being studied if the participant was merely a passenger in a car driven by someone else. Adverse events are measured in both the group taking the medication in a placebo-controlled trial and in the placebo group. In this way it can be determined if the events are related to the medication. A statistically higher rate in the medication group would imply that the adverse events are related to the medication.

In contrast, an adverse effect is a health consequence that is known or presumed to be due to the medication being studied. Generally an adverse effect is distinguished from a side effect by the seriousness of its effect on the body. Side effects are expected but unwanted effects that are frequently managed without discontinuing the medication. If discontinuation becomes necessary, a side effect usually resolves without specific treatment. Adverse effects, in contrast, are uncommon effects that pose more risk to the patient. These are more likely to necessitate discontinuation of the medication and further specific treatment to resolve. Safety of medications is about adverse effects. Tolerability is about side effects.

Side Effects

The studies cited in this report are based on a ten-year literature review from June 1, 2000 through May 31, 2010. As discussed in more detail in the Appropriateness section, this review includes all papers describing pediatric double-blind controlled trials identified through the literature search along with all open label studies of at least 20 patients and at least 8 weeks duration.

First generation antipsychotics (FGAs) and second generation antipsychotics (SGAs) cause many of the same common side effects, although the rates at which these are experienced may differ. These unwanted effects generally fall into the following categories: sedation/fatigue/somnolence, increased appetite/weight gain, nausea/vomiting/dyspepsia/drooling, dry mouth/blurred vision/difficulty urinating (anticholinergic effects), restlessness (akathisia), and increased prolactin levels. Many of these are managed by lowering the dose of medication, changing when and how the medication is given, changing food or water intake, adding another medication, or watchful waiting. Any of these side effects can become an adverse effect if they occur for prolonged times, occur at an intense level, fail to respond to management listed above, or are intolerable to the patient.

Generally, all the available studies of antipsychotic medications in children and adolescents found that both SGAs and FGAs were relatively well-tolerated. (See Tables A–I.) SGAs, however, are reported to be better tolerated than FGAs.[8,9] This implies that side effects (as well as adverse effects) are generally fewer in number, fewer in type, less intense, or differentially experienced by children and adolescents taking SGAs as compared to FGAs. There have been very few direct comparisons of these medications that would allow reliable measurement of how tolerability compares, but one in adults shows that adherence rates for SGAs are higher than FGAs during short-term treatment.[9] Adherence refers to whether the medication is taken as prescribed. When side effects are noticeably unpleasant to the patient or interfere with functioning, the medication is less likely to be taken as directed or may not be taken at all. Increased adherence for SGAs implies that patients tolerate these medications better.

An example may serve to clarify the importance of tolerability. SGAs frequently increase appetite and weight gain. FGAs commonly cause muscle restlessness. In the short run, a patient may not notice the appetite change or weight gain because it does not create any actual bodily discomfort. Motoric restlessness, however, can be extremely unpleasant. Hence the patient on the FGA may not take the medication as often as prescribed. This is in spite of the fact that the long-term consequence of increased appetite/weight gain may actually be more uncomfortable and harmful to health than restlessness. Lower adherence for the FGAs makes them less effective.

Adverse Effects

As noted previously, an adverse effect is an unanticipated negative effect of a medication. Antipsychotic medications have been linked to a number of adverse effects that fall

naturally into five general categories: obesity/metabolic, neuromuscular, hyperprolactinemia/reproductive, cardiac, and white blood cell effects. Other effects would be very rare and will not be discussed here. Generally, it is seen that children and adolescents experience the same adverse effects as adults on antipsychotics, but at a higher rate.

Evidence from the Ten-Year Literature Review

Obesity/Metabolic Adverse Effects

The side effect of increased appetite/weight gain is common for FGAs and SGAs and can naturally lead to obesity. Additionally, the population with mental disorders tends to have higher weights even when not taking medication.[10] The youth pattern of weight gain with these medications generally follows the pattern noted in adult studies. Olanzapine is widely noted to cause the most weight gain and BMI (basal metabolic index) change of the SGAs followed by quetiapine, risperidone, and aripiprazole in that order.[11] Overall, 10 to 36 percent of children can become overweight after only 3 months of treatment with antipsychotics.[11]

In short-term pediatric studies, the SGA olanzapine has caused more weight gain than two FGAs, haloperidol and molindone[12 (I-3)]. Risperidone and haloperidol did not differ in the amount of weight gain.[13(I-9), 14(I-15), 15(I-16)] After one year, weight gain with risperidone appeared to stabilize over the next two years with modest increases mostly representing normal growth rates.[16(B-34)] The longest olanzapine study in youth showed mean weight gains over one year of about 28 pounds.[17(C-7)] Over 18 months, an adult study showed perphenazine and ziprasidone caused net weight loss compared to olanzapine, quetiapine, and risperidone.[18]

Obesity can lead to metabolic syndrome, which increases the risk of cardiovascular disease and diabetes. Metabolic syndrome consists of obesity, changes in blood lipids, hypertension, and elevated blood glucose. In one short-term SGA study that focused on these changes in children, lipid changes were more prominent than glucose changes and full metabolic syndrome and diabetes was rare.[11] Olanzapine was again the worst offender causing more glucose changes than the others and negatively affecting all types of blood lipids but one. Quetiapine and risperidone did not have much effect on glucose levels but did increase one blood lipid, triglycerides. Quetiapine further affected other lipids and had overall broader metabolic effects. Aripiprazole was not associated with any changes. This study further found that children do not gain proportionally more weight than adults on these medications. There are no studies specifically looking at these metabolic changes in youth taking FGAs.

Overall the SGAs olanzapine and quetiapine are more likely to cause weight gain than the FGAs molindone, haloperidol, and perphenazine. Overall, aripiprazole, ziprasidone, and perphenazine appear to pose the least risk for weight gain, obesity, and metabolic syndrome. Risk for weight gain with risperidone appears to be intermediate between these two groups. Weight gain can generally be minimized if scrupulous attention is paid to caloric intake and activity level, but that can be a challenge, particularly in youth with

mental health disorders.

Neuromuscular Adverse Effects (EPS/TD//NMS)

Children and adolescents are generally thought to be more sensitive to the neuromuscular adverse effects of antipsychotics such as extrapyramidal symptoms (EPS) and tardive dyskinesia (TD).[19] Extrapyramidal symptoms commonly consist of muscle cramping, involuntary movements, extreme restlessness, and a syndrome similar to Parkinson's disease with muscle rigidity. When EPS appear, the medication dose is frequently lowered or another medication is added to address the symptoms. In many short term and intermediate term studies of SGAs there are few to no instances of participants experiencing any of these muscle problems. (See Tables A-G, I.)

In long-term studies of risperidone up to 3 years about 10 percent of the children experienced EPS muscle effects at one point or another.[20(B-28), 16(B-34), 21(B-36)] Ratings of these problems tended to decrease over time.[22(B-39)] Olanzapine and quetiapine generally did not cause these problems even in studies up to one year for olanzapine.[17(C-7)] In direct comparison, risperidone caused more EPS than olanzapine.[23(I-4)] In short term studies, ziprasidone and aripiprazole appeared to cause more EPS, especially extreme restlessness, in rates up to 10 percent for aripiprazole and up to 22 percent for ziprasidone.[24(I-13), 25(F-9), 26(E-2)]

The FGA molindone caused moderate to severe EPS in 18 percent of youth in one study.[12(I-3)] Although this rate is similar to the rates in ziprasidone and aripiprazole, it should be noted that ziprasidone and aripiprazole only caused EPS in the mild to moderate range. Haloperidol caused more severe EPS than risperidone in short term studies,[14(I-15), 13(I-9)] while in a longer term study the difference was not apparent.[15(I-15)] In adult studies perphenazine caused more EPS than risperidone, olanzapine, quetiapine, and ziprasidone.[18]

Tardive dyskinesia (TD), a movement disorder that can appear months to years after being on a medication, was rare in studies; this may be due to part to the fact that most of the studies were too short to capture the incidence of TD. A review of 10 SGA studies turned up 3 cases in 783 youth, 2 of which resolved after medication discontinuation.[27] As TD is irreversible, these 2 cases are most likely not TD but rather just EPS. Studies of FGAs for TD in youth do not exist although by extension from adult studies they cause TD at higher rates than SGAs.

Neuroleptic Malignant Syndrome (NMS) is a rare, acute medical crisis consisting of fever, muscle rigidity, vital sign instability, and confusion. Risk for this rare condition is generally not predictable. It is similar to other conditions with hyperthermia such as encephalitis, heat stroke, and anesthetic malignant hyperthermia. It is known to affect males more than females and is thought to have a genetic component. Early detection, rapid cooling of the body, and supportive measures are key in treatment. No study reported any instance of NMS. NMS usually occurs in the first few weeks of treatment, and although it was not reported in any of the studies reviewed, it has shown up in case reports and can be lethal.

Patient profile from STAR Health psychotropic medication utilization review process

Case #2: 3-year old female who has recognized pervasive developmental delays, hyperactivity, and disruptive behavior towards same age children, younger children and adults at daycare. She will not follow directions. Loud noises appear to hurt the child's ears. Changes in the daycare activities cause her to hide and rock back and forth. When she is not hitting other children, she is piling up toys by color, screaming and grunting, and trying to leave the daycare room. Several times she has managed to get out of the daycare, and was found outside near the street. The physician tried Dexedrine® spansules sprinkled on pudding to reduce hyperactivity, but this appeared to cause increased irritability/anger. Low dose risperidone was started because it is available in a liquid. The child is now able to sit in groups, and her impulsive aggression has decreased.

Psychological factors in this case include anxiety with change in routine and compulsive behaviors which can be due to both exposure to abuse, neglect and developmental problems. Psychiatric/behavioral symptoms include probable sensory integration disorder, agitation/impulsive aggression, associated with pervasive developmental delays/autism.

The choice to treat this child with atypical antipsychotic medication is based on the severity of the symptoms and the impact of those symptoms on the people around her. In this case, there is an additional factor of safety since she is getting out of the daycare. The use of an atypical antipsychotic medication could be the first choice since she has pervasive developmental disorder (PDD) and medications are approved by the FDA to treat PDD, or it can be used after other medications have been tried. As illustrated in this case, the choice of medications can also be influenced by the age and ability of the child to swallow medications.

In summary, of the antipsychotics for which any data is available, haloperidol and molindone (which has since been withdrawn from the market) cause the most severe EPS. Rates for aripiprazole, ziprasidone, and risperidone are in the next category of risk, and olanzapine, quetiapine, and presumably clozapine (due to its similarity to olanzapine) are least likely to cause EPS and TD. Overall rates for incidence of EPS over the course of treatment ranges from close to 0 percent with low risk drugs, to about 10 percent for moderate risk drugs, and 20 percent or higher for high risk drugs. Risk of EPS appears to diminish with time on a drug while risk for TD increases over time. Youth rates for TD with SGAs are unknown at this time since most studies were too short capture the incidence of TD. Based on the available short-term studies, TD rates for SGAs are extremely low. Rates for FGAs are not generally known although they are presumed to be higher based upon adult studies.

Hyperprolactinemia/sexual maturation

Prolactin is a hormone secreted by the pituitary gland that stimulates the human breast to produce milk. Most antipsychotics interfere with the regulation of production of this hormone causing prolactin blood levels to rise. Many studies of SGAs have noted rises in blood prolactin levels (See Tables A-G, I). In the vast majority of these studies, there are no clinical symptoms. After discontinuation of antipsychotic medication, prolactin levels return to normal.

Although high prolactin levels can produce breast changes such as increase in size, pain, or milk production, studies in youth have failed to correlate the amount of medication and the presence of clinical symptoms. Other possible effects include cessation of menstrual

periods, lack of sexual desire, and erectile dysfunction. These side effects typically are not noted in the prepubertal population and, unless specifically addressed, can go undetected in adolescents.

Studies have found some antipsychotics cause more prolactin increase than others in the following order:
risperidone/paliperidone>haloperidol>olanzapine>ziprasidone>quetiapine>clozapine> aripiprazole.[10, 28(I-8), 13(I-9)] Aripiprazole causes prolactin levels to fall.[29(F-6), 30(F-8), 10] Blood levels of prolactin tend to rise in the first few months of treatment and then decline as treatment continues.[31(B-12), 28(I-8)] Most elevations are relatively mild and in one moderately large uncontrolled study 12 percent of youth reported changes in sexual functioning or menstrual/breast problems.[28(I-8)] It must be kept in mind that untreated populations also experience symptoms in these areas.

In summary, increase of blood prolactin with antipsychotics is common, generally produces few if any symptoms, and self corrects over time. For this reason, monitoring of blood prolactin levels is not recommended for youth taking antipsychotics. Risperidone and paliperidone produce the most increase and aripiprazole produces a decrease. Other antipsychotics are intermediate in effect. The long-term effects of antipsychotics on sexual development in youth are unknown because the available studies are short-term (up to three years in duration).

Cardiac Adverse Effects

Antipsychotics can affect the heart by slowing down its electrical recovery or repolarization after a heartbeat. This shows up in an electrocardiogram (ECG) as lengthening of a certain part of the tracing called a QT interval. This effect, called QTc prolongation, can lead to a potentially fatal arrhythmia known as torsade de pointes. The vast majority of pediatric studies do not show any clinically significant changes in the ECG for youth on antipsychotic medications. (See Tables A-I.)

In one study, ziprasidone was associated with prolongation in 3 out of 20 patients to a level considered above normal.[32(E-3)] The amount of lengthening did not appear related to the amount of the medication. This study also documented that automated ECG readings may miss QTc prolongation; therefore ECGs should be read by cardiologists in patients taking ziprasidone or otherwise at risk rather than depending upon computer interpretation. Torsade de pointes did not occur to any youth participating in any study of antipsychotics meeting review criteria in the ten-year review period.

Clozapine has been associated with myocarditis, an inflammation of the heart, but incidence in children has been reported to be very low. Because of other problems with clozapine, this medication is used in only very select circumstances when other medications have failed to adequately treat symptoms of schizophrenia.[33,10]

White Cell Decreases

Clozapine is associated with a decrease in the amount of infection fighting white blood cells, called neutropenia, or a complete failure to produce white cells, called

agranulocytosis. The risk is significant and in the case of agranulocytosis can be fatal. According to one retrospective study, the risk over one year of treatment for neutropenia was 13 percent and the risk of agranulocytosis was 0.6 percent.[34] Generally, discontinuing the medication can return levels to normal if they have not fallen dangerously low and patients frequently are able to successfully restart clozapine. Agranulocytosis generally requires permanent discontinuation of the medication, particularly in outpatient settings. For these reasons, clozapine is reserved for youth with schizophrenia who have not responded to other medication. Its use requires regular monitoring of white blood cell levels.

Adverse Event Reporting

MedWatch,[35] established by the FDA in 1993,[2] collects voluntary reports from professionals and consumers about adverse experiences with drugs and other entities regulated by the agency. This database is public and can be downloaded by anyone, but presents insurmountable problems for interpretation. The problems with this database[36] and why it cannot be used to determine rates or types of adverse effects with medications are:

1. Reporting is voluntary—this assures that the data is an undercount of adverse effects with medications.
2. Anyone can report—this assures that there are duplicate sets of data in the file that cannot be culled because identifying information is not available.
3. Data can be reported incompletely—this assures that demographic data is missing in many cases, complete information on medications taken is missing, and outcomes are not always recorded.
4. Correlation is not causation—reports show that many persons were on multiple medications at the time of the adverse event and there is no means of determining from the data whether the adverse event was due to a specific medication, a combination of medications, or not due medication at all
5. There is no accurate denominator from which to calculate rates—there is no national count of the numbers of persons who took a given medication and did not experience an adverse event.
6. Data set is not user friendly—the data set is structured so that it requires programming knowledge to aggregate in a meaningful way; and it can easily be misinterpreted.

The FDA and the scientific community know well the shortcomings of MedWatch. Because of these difficulties, the true incidence of post-marketing adverse events for medications is mostly unknown unless separate studies are undertaken to determine them. Even this can be fraught with problems as exemplified by the black box warning added for use of antidepressant in youth on the basis of increased suicidality. This adverse event was generally misinterpreted as an actual increased rate of suicide even though no clinical trial ever documented any youth suicide as a result of taking antidepressants.[37] For rare or very late-appearing adverse events, post-marketing studies would have to be

extremely large and/or extremely long-running to produce valid data from which rates could be calculated.

Discussion and Summary

Overall, the scientific evidence base as reflected in the literature review (Tables A-I) show that the most significant overall adverse effect for second generation antipsychotics is their propensity to cause weight gain and sedation. Weight gain carries an attendant risk of metabolic syndrome, and later heart disease and diabetes. The National Institute of Mental Health (NIMH) is currently sponsoring a 5-year study, Metabolic Effects of Antipsychotics in Children (MEAC), which may provide more answers about risks in this area.[38]

In the meantime, weight gain should be addressed by attention to caloric intake, healthy diet, and exercise, and the risk for metabolic syndrome should be carefully monitored. Regular glucose and lipid screening is recommended although studies show that many children in state Medicaid programs do not get these screenings.[39] Medicaid children and youth face various challenges to receiving periodic screening services, such as lack of transportation and lack of flexibility in their parents' work schedules. Nevertheless, parents and patients should understand the potential side effects of these medications and the importance of diet, exercise, and periodic screenings to reduce the risk of adverse effects.

Although the sedation encountered with both FGAs and SGAs is a troublesome adverse effect, the risk of sedation pales versus the benefit of amelioration of severe symptoms for many families. In many cases it wanes without specific intervention as the body adjusts to the medication. Fortunately the few studies that looked at cognition did not show any negative effects and even indicated some possible positive effects in this area.

First generation antipsychotics carry more risk of neurologic (EPS) and anticholinergic side effects and a later risk of tardive dyskinesia (TD) than SGAs. EPS and anticholinergic effects require adjunctive medication, dose manipulation, and/or time to subside. Regular screening for the development of TD should be performed although screening frequency may be low in this population.

Children and adults alike generally find neurologic and anticholinergic side effects more immediately unpleasant compared to weight gain and sedation. In essence, parents and practitioners must make decisions about the trade off between these two types of adverse effects when choosing antipsychotic medications.

But, as the studies show, most patients tolerated the medications well and most did not discontinue them. Most adverse events in clinical trials were transient and mild. Selected properly after careful assessment, with ongoing screening for adverse effects, and for short term treatment perhaps up to three years, antipsychotics appear safe in select preschool, school age, and older children. (See Section V- Appropriateness for discussion of very young children and antipsychotic use.) Long term effects, however,

are ultimately unknown for the SGAs and the FDA MedWatch system is inadequate to uncover them reliably.

V - Appropriateness

Determination of Appropriateness

Standard of Care

"Standard of care" is a legal rather than medical term. It refers to the degree of skill, care, and diligence that is expected to be exercised by a member of the same profession under the same conditions. It is not a static level of care quality attached to a diagnosis, but varies according to the time, place, and clinical circumstances of the patient and care encounter. Capabilities of the family to participate in care, resources in the community to provide care, and youth willingness to participate can also affect the standard of care in that encounter.

Legally, care that is in accordance with the "standard of care" is considered appropriate care. By this "standard of care" measure, the general use of antipsychotics in pediatric populations for schizophrenia, bipolar disorder, autism, tics, and aggression associated with many disorders is appropriate. Medications of this class have been used for these disorders in youth for a long time and physicians are trained and expected to use them for these indications in children and adolescents by their professional colleagues.

Evidence Based Medicine

Evidence based medicine assumes that clinical decision-making should be based on the best available scientific information. In an ideal world the "standard of care" reflects the scientific evidence base, but evidence constantly changes and it can take years for new information to be fully integrated into clinical practice. Four levels of evidence for treatment in order from most rigorous to least are:

1. Randomized double-blinded controlled trials (RCTs)
2. Prospective open label studies (POLs)
3. Retrospective chart reviews, case series
4. Single case reports, anecdotes

Randomized Controlled Trails

Studies required for FDA approval must be randomized double-blinded placebo-controlled studies (RCTs), i.e. research of the highest scientific quality. A controlled study compares one treatment to another treatment or no treatment. In the case of the most rigorous drug research, a placebo (pill without active ingredients) is used for comparison. Participants in the study are given either the active drug or the placebo. In double-blinded research neither the participants nor the researchers know whether active treatment or placebo has been given until the end of the study. This ensures that the data the researchers gather during the study is unbiased and as objective as possible.

Additionally, whether a participant receives a placebo or the active drug is determined by chance, i.e. it is random, further ensuring validity of the conclusions of the study.

Once the study has ended, researchers analyze data with knowledge of who has received active treatment and who has received placebo. A drug is considered effective if it produces significantly more positive effects than placebo for the condition being treated. Generally, placebo effects themselves can be quite large. Especially in teenagers, up to a third or more of participants in drug studies routinely have a positive response to placebo. The standard of determining efficacy of any given medication in RCTs is therefore quite high.

Prospective Open Label Studies

Prospective open label studies (POLs) involve less rigorous scientific evidence. This research is not controlled, i.e. does not have a placebo or other comparison group. The participants and researchers know what medication is being used. These studies use standardized assessments and data collection methods to ensure some measure of objectivity. There is no way to know, however, if the medication is more effective than placebo in this instance. The data collected may be biased. These studies, if positive, therefore *suggest* efficacy but do not prove it. These studies are frequently performed before doing more rigorous double-blinded placebo controlled studies because they are less expensive and quicker to perform. If these studies produce positive results, then it is reasonable to proceed with the longer, more expensive RCTs.

Retrospective Chart Reviews, Case Series

Retrospective chart reviews and case series study data after the fact. Researchers collect data from existing clinical records not originally created for research purposes. No randomization, no assurance that the treatment or clinical documentation was performed in a comparable manner, and no control for bias exists. If retrospective reviews produce a positive pattern, then POLs may be in order.

Single Case Reports

Single case reports are anecdotes. These do not constitute data from which any conclusions can be drawn. Their value lies in alerting a reader or listener to the possibility of a connection that then might show up in a series of cases. A series of cases could lead to a retrospective review that might provide evidence that performing a prospective open-label study is reasonable.

The ten-year literature review of antipsychotic use in children and adolescents that accompanies this paper includes only RCT and select POL data (at least 20 patients and at least 8 weeks duration). (See the Methods section below for a more detailed description of the literature review methodology.)

Guidelines, Pathways, Parameters

Individual practitioners do not have the time to review all the burgeoning relevant research produced on a given clinical topic. Thus, professional groups organize formal reviews of the research literature and publish their findings as practice guidelines, pathways, or parameters. They provide guidance on what clinicians should address in the treatment process and what is known to be effective at the time of publication.

The American Academy of Child and Adolescent Psychiatry (AACAP) has published practice guidelines for some psychiatric disorders affecting youth. Recent ones that sanction the use of antipsychotics to varying degrees are parameters for schizophrenia (2001), bipolar disorder (2007), depressive disorders (2007), oppositional defiant disorder (2007), and posttraumatic stress disorder (2010). Each of these documents was developed by expert review of the best scientific evidence available at the time of publication in conjunction with expert clinical consensus. Recommendations regarding antipsychotics from these AACAP practice parameters are:

Patient profile from STAR Health psychotropic medication utilization review process

Case #3: 3 ½ year old male with history of shaken baby syndrome, intracranial hemorrhage, seizures, who is on a ventilator. This child is responsive to others at times, but has frequent periods of agitation. He has poor swallowing reflex and is fed through a tube in his stomach. During these episodes of agitation he will pull at the ventilator hoses and attempt to pull out the tracheotomy tube. When he is like this, his hands need to be tied to the bed.

This case represents the off label use of antipsychotics in a medical setting for delirium and to reduce agitation associated with a brain injury rather than for psychological reasons. The use of sedative hypnotics (Ativan®, Valium®) has the potential to suppress the breathing centers of the brain making it difficult to assess the need for ventilator support. Sedative hypnotics can also make this child more agitated and increase delirium.

Schizophrenia[40]

"Antipsychotic agents are recommended for the treatment of the psychotic symptoms associated with schizophrenia."[40, p.5S] This recommendation is identified as a minimal standard, meaning that it is considered the general standard of care and only rarely would it be appropriate to deviate.

Bipolar disorder[41]

"Although more controlled trials are needed, mood stabilizers and atypical antipsychotic agents are generally considered the first line of treatment."[41, p.107] This pharmacotherapy is considered a minimal standard, meaning it is considered the general standard of care and rarely would it be appropriate to deviate.

Depressive disorders[42]

"Although there are few studies in youths... it appears that the combination of antidepressants with antipsychotics may be helpful for patients with psychotic depression."[42, p.1518] This recommendation is identified as a

clinical guideline, meaning that it is a standard that applies most (~75 percent) of the time.

Oppositional defiant disorder (ODD)[43]
Antipsychotics along with mood stabilizers are noted as adjunctive treatment for aggression in ODD. This recommendation is part of a clinical guideline, meaning that it is a standard that applies most (~75 percent) of the time. In this particular parameter the context is that it would be used if front line psychotherapies and environmental interventions had failed to sufficiently decrease aggression or the severity of the aggression required an intervention with more immediate results.

Posttraumatic stress disorder (PTSD)[44]
Antipsychotics "may….decrease some PTSD symptoms", such as flashbacks and hallucinations.[44, p.425] This recommendation is identified as an option, meaning that it can be acceptable practice. Options are generally used when standard treatments have failed to effect needed improvements. In the case of PTSD, psychotherapies are first line treatment and antidepressants would generally be tried before antipsychotics if medication became necessary.

Guidelines also exist for the treatment of aggression. Unlike other disorders, aggression is not a diagnosis, but rather a symptom that can be found in many psychiatric conditions. The Treatment Recommendations for the Use of Antipsychotics for Aggressive Youth (TRAAY) Part I[45] found that high quality research data was scarce as of 2003. Part II[46] recommended the use of antipsychotics for aggression based upon available data and expert opinion at that time. In general, this guideline recommends that psychosocial treatments for aggression be tried first. Treatment of the primary disorder should also occur and if medication is appropriately part of treating that disorder, then this should proceed before medication directly targeting aggression. Lastly, if these measures fail, antipsychotic medication is then recommended if the severity of the aggression requires it for safety and quality of life.

The TRAAY guidelines specified that second generation antipsychotics were the first line choice, but much more experience and research on antipsychotics in youth has accumulated since that time. Recently, a collaborative effort of academic, non-profit, and government entities has completed a new guideline, "Treatment of Maladaptive Aggression in Youth" (T-MAY) set for publication later this year.[47] Although the complete paper based upon recent research has yet to be published, the T-MAY Pocket Reference Guide based upon this work is available.[48] T-MAY, similar to TRAAY, recommends psychosocial treatments and medication for the primary disorder first. If these have failed to produce necessary reductions in aggression, then trials of antipsychotic medication are warranted. This guideline no longer specifies using second generation antipsychotics over first generation agents.

The evidence summarized in the clinical guidelines presented here generally supports the use of antipsychotic medications as primary treatment for youth with schizophrenia and bipolar disorder, for psychosis in depression, and as adjunctive treatment for aggression in a variety of disorders.

Evidence from the Ten-Year Literature Review

Introduction

The primary research evidence base changes constantly, but more research has been done on antipsychotics in youth in the last ten years than occurred in all previous years combined. The overwhelming majority of research in this area addresses the second generation antipsychotics (SGAs), with the first generation only appearing in comparison studies. Risperidone, the oldest SGA except for clozapine, has accumulated more research studies than any other. The following describes the last ten years of antipsychotic medication trials up through patient age of 18 years old. Every clinical trial paper reviewed is covered in the attached tables. This constitutes the majority of the scientific evidence base from which clinical care derives its guidance on prescribing antipsychotics in youth.

Methods

A search of the peer-reviewed professional literature from June 1, 2000 through May 31, 2010 was conducted through the federal public access Gateway website. This website accesses the Medline database of medical literature in conjunction with the National Library of Medicine. The search addressed the following second generation or atypical antipsychotic medications currently available through the Texas Medicaid vendor drug program: aripiprazole, clozapine, olanzapine, quetiapine, risperidone, ziprasidone, iloperidone, paliperidone, and asenapine. It also addressed the following first generation or typical antipsychotic medications also available to Texas recipients of Medicaid: chlorpromazine, haloperidol, molindone* (this medication was withdrawn from the market and no longer available after June 30, 2010), perphenazine, pimozide, thioridazine, thiothixene, fluphenazine, and trifluoperazine. Papers addressing adult studies or studies that combined adults with children and/or adolescents were generally excluded. Following the methodology of Jensen[8], all papers describing double-blind controlled trials identified through this search were included in this review along with all open label studies of at least 20 patients and at least 8 weeks duration.

Results

The literature search identified more than 200 pediatric clinical trials published in English. Fifty-two papers on double blind, randomized controlled trials (RCTs) and 48 prospective open label studies (POLs) met criteria for this review. Eighteen studies included above compared one antipsychotic with another and are listed and described separately.

PEDIATRIC CLINICAL TRIALS FOR SECOND GENERATION ANTIPSYCHOTICS

Clozapine (Table A)

Clozapine (CLZ) was the first second-generation antipsychotic to become available in the United States. Marketing approval was obtained in 1989 for treatment resistant

schizophrenia in adults. Hailed as a breakthrough, this drug was able to improve symptoms in patients who had shown little to no response previously to any treatments—medication, behavioral, or psychotherapeutic. In 2002, regulatory permission was gained for marketing it for preventing suicidal behavior in schizophrenia and schizoaffective disorder. Unfortunately, these improvements came at a price; clozapine can cause serious white blood cell decreases that leave patients dangerously open to infection. It can also cause seizures and serious inflammation of the heart. There are currently no FDA marketing indications for clozapine in the pediatric age group.

The ten-year pediatric literature review only identified 2 RCTs and 2 POLs that addressed clozapine. (An expanded search identified one further RCT prior to the review period not included for review.) Both RCTs and 1 POL are studies that compare clozapine to olanzapine (OLZ) for symptoms of schizophrenia.[49(I-7), 50((I-10), 51(I-12)] The other POL is a clinical trial from 2005 that studied the effect of clozapine on aggression in pediatric schizophrenia.[52(A-1)] In all these studies, clozapine was found to have a positive effect on the symptoms of pediatric schizophrenia in children as young as 7 years old and for study periods as long as 24 weeks. Superiority of clozapine to olanzapine was not demonstrated except for treatment of negative symptoms in those children who were considered treatment resistant.[50(I-10)] (In the RCT from 1996, clozapine was clearly superior to haloperidol for both positive and negative symptoms in refractory pediatric schizophrenia.[53])

Summary Since clozapine was introduced in 1989 and went generic prior to the ten-year period reviewed for this study, few studies of clozapine met review criteria. Because of the risk of serious side effects, the available literature only supports the use of clozapine for pediatric patients with treatment-refractory schizophrenia (i.e. those patients who have not responded to other antipsychotic medications) and whose negative symptoms are a prominent feature affecting their functioning. Gogtay, et al, in their 2008 review of the literature on the pediatric use of clozapine concluded: "Clozapine remains the most effective medication for treatment refractory cases of COS [childhood onset schizophrenia] both for short-term and maintenance treatment."[33] Other experts in the field agree that although not approved for marketing, clozapine definitely has a place in the treatment of pediatric schizophrenia.[54]

Risperidone (Table B)

Risperidone (RIS) is a second generation antipsychotic medication first approved for marketing for acute adult psychotic disorders in 1993. It was the second medication in this group to come on the market after clozapine in 1989. In 2002, its marketing approval was extended to long term treatment of adult schizophrenia. Monotherapy and adjunctive therapy of acute adult manic and mixed episodes in bipolar disorder were approved as marketing indications in 2003. Acute and maintenance treatment of irritability in autism for ages 5-16 was added in 2006 based upon three RCTs.[55(B-24),56(B-19),57(B-37)] The treatment of pediatric schizophrenia (ages 13-17 years) and pediatric bipolar I disorder (ages 10-17 years) were added in 2007 based upon 2 RCTs[58] (second not yet published) and 1 RCT[59] respectively.

The ten-year literature search identified 59 clinical trials papers that met criteria. Forty five papers documented 25 RCTs and 21 POLs. (Fourteen other papers addressed trials that compared 2 or more antipsychotic medications. Comparison trials are covered in a

separate section after single medication sections.) Some papers analyzed complex studies that had both RCT and POL components and some papers documented new analyses of data from previously published trials. By a wide margin, more pediatric clinical trials have been published about risperidone than have been published about any of the other antipsychotics. Over the ten years of the review period, risperidone has been intensively studied in autism and disruptive behavior disorders with only 5 trials being devoted to other diagnostic categories. Table B references for this body of work are summarized in Figure 1 below.

Figure 1
Risperidone Clinical Trials Summary

Risperidone Trial Population	Tot #	Ages	RCT Study references Numbers refer to Table B	POL Study references Numbers refer to Table B
Disruptive behaviors (DB)				
Disruptive behavior disorders	5	5-17	1,6,13	28,36
DB + low IQ	15	4-15	4,11,16,17,20,21,22,23,26,27	34,39,42,21,43
DB + epilepsy	1	2-18		31
Autism (ASD)				
Autism disorders	19	2-17	5,8,32,9,10,12,15, 37*,18,19*, 24*	32,12,35,37*,18,41,44, 45
ASD Lab/nutrition studies	2	5-17	7,14	14,40
ASD + Down syndrome	1	3-12		29
Schizophrenia spectrum	1	13-17	2*	
Bipolar disorders	3	4-17	3*	33 ,38
Tic disorders	1	7-17	25	
Mixed dx (LFTs)	1	3-17		30

*Studies that led to FDA approval for pediatric marketing indications

Risperidone was found to be more effective than placebo in treating disruptive behavior disorders, including severe aggression, in children with lower than average intelligence (See Fig. 1).[60,61,62,63,64,65,66,67,68] This was born out by more than five RCTs that totaled several hundred participants and included children as young as 5 years and as old as 15. (Indeed it is approved for this indication in some other countries.[63]) Positive effects were maintained up to 3 years in POLs for children as young as 6.[21,16,22] One POL suggests that it is effective in ages as young as 2 years old for children with seizures and disruptive behaviors—without having any adverse effect on seizure frequency. At no time was any decline in cognition, including memory, demonstrated with use of risperidone.[69,70] Some positive cognitive benefit was shown in several areas in one study.[70] Throughout all these studies risperidone was well tolerated, although weight gain was noted in many of them.

Risperidone was more effective than placebo for treatment of irritability and disruptive behaviors in autism for ages 5 to 16.[70,71,72,73,57,56,55] This, of course, is reflected in FDA marketing approval for this indication. It was effective for maintenance of these treatment gains as shown by several RCTs and POLs for as long as 6 months for children from 2 to 17 years old.[73,74,75,76,77,78] Discontinuing risperidone generally led to a return of disruptive behaviors.[79,80] One POL suggested it was also effective in children aged 3-12 years with autism combined with Down's syndrome where it decreased aggression, self-injury, social withdrawal, and sleep problems.[81] Again, overall no detrimental effect was found on cognitive performance and risperidone might even enhance memory in autism.[70,79] Studies of blood prolactin levels in the population with autism showed that although levels increase up to 4 times the normal level in the first 2 months of treatment, these levels generally return to near normal over the next 3 to 5 months.[31] Nutritional balance was not affected although weight gain remained a problem for children with autism being treated with risperidone.[82,83] Studies of the pattern of weight gain showed that it tended to be greatest in the first 2 months of treatment and then decelerate over time.[84,83] Generally risperidone was very well tolerated by children with autism,

although the core social symptoms in this disorder were rarely improved by risperidone treatment.

Patient profile from STAR Health psychotropic medication utilization review process

Case #4: 10-year old male with ADHD, combined type and bipolar disorder, mixed episodes with psychosis. This youth has had multiple psychiatric hospitalizations for physical aggression at home and at school. This child reports he is "bad" because he "hears bad voices" and "something is wrong with his brain." He has been treated with medications for ADHD, which help with focus and concentration, but he remains irritable, aggressive and will alternate between being withdrawn and being afraid of others who "are looking at him." He has stated that he should be able to live by himself, and has tried to get in the car and drive away to be on his own. This child stays awake at night pacing because he is scared and the voices are worse at night. Past medication trials include Ritalin®, Adderall®, lithium, and Depakote®. The antipsychotic medication aripiprazole was added to his night-time medication regimen, and after a few weeks his impulsive aggression and mood instability have improved. He no longer hears "bad voices" but he is still afraid of the dark. He has been able to sleep most of the night.

Psychological problems and psychiatric symptoms include anxiety, depression, mood instability, psychosis (hearing voices, paranoid and grandiose thoughts) and impulsive aggression. This child has been tried on several medications as mood stabilizers (lithium, Depakote®) with poor to minimal improvement. The use of antipsychotics in this case is warranted due to the symptom severity and the antipsychotic medication can have multiple actions - it can reduce anxiety, depression, and psychosis and act as a mood stabilizer. Not using an antipsychotic medication could result in this child being prescribed three or four other medications which have a higher risk profile than the antipsychotic medications.

As noted previously, few clinical trials have been done with risperidone in other disorders during the review period. One RCT each found risperidone more effective than placebo for schizophenia[58] and bipolar disorder.[59] These trials are the basis for FDA marketing approval for these two indications. POLs suggested that efficacy reaches down at least to age 6 for monotherapy with risperidone in bipolar disorder[85] and down to age 4 when added to lithium in those children who failed to have an adequate response to lithium alone.[86] Risperidone was shown to be equal in efficacy to clonidine in one comparison RCT in the treatment of tic disorders in children aged 7-17 years.[87] A general POL study of liver function testing during risperidone treatment showed that blood liver enzymes do increase during treatment, rarely to marked levels at therapeutic doses, and that these changes are largely asymptomatic.[88]

Summary Risperidone is the most studied antipsychotic in child psychiatry. It has FDA marketing indications for acute and maintenance treatment of irritability in autism (ages 5-16), schizophrenia (ages 13-17), and bipolar disorder (ages 10-17). The literature shows further effectiveness for a wide variety of disruptive behavior disorders such as conduct disorder, oppositional defiant disorder, and attention deficit hyperactivity disorder as well as autism. The literature is robust for efficacy in these disorders even when they are associated with lower intelligence and suggestive of efficacy even when epilepsy and Down's syndrome are present. Risperidone has been used in clinical trials with patients as young as age 2. The literature suggests that it is safe and occasionally effective at this age for behavioral improvement. Risperidone, similar to other antipsychotics, has not been shown to be effective in treating the core social deficits in autism. Weight gain consistently occurs in clinical trials with risperidone. The most rapid weight gain occurs early on and is not associated with a change in nutritional balance. Higher blood lipid levels are also seen as well as higher levels of prolactin. Prolactin levels are not usually

associated with any increased clinical symptoms in sexual or reproductive organ function and drift back toward normal over a period of 3 to 5 months. Transient increases in blood liver enzyme levels are also seen, though clinical symptoms are rare. Risperidone can also cause movement disorders although lower doses cause this less frequently and appear just as effective for treating symptoms. Risperidone was not shown to adversely affect cognitive function. It may even improve some aspects of cognition as well as sleep in selected children.

Olanzapine (Table C)

Olanzapine (OLZ) is the second generation antipsychotic most closely related to clozapine. Pharmacologists hoped to retain the effectiveness of clozapine in treating negative symptoms and refractory schizophrenia, while dispensing with the high risk of serious side effects such as decreased production of white blood cells. In some measure this medication has succeeded in achieving those goals. It was approved for the U.S. in 1996 for the marketing indication of psychosis in adults and was the third medication available in this group. In 2000, manic and mixed episodes in bipolar disorder and maintenance treatment in adults were added as marketing indications. Combination with lithium or valproate to treat acute mania was added in 2003. Long term treatment for bipolar I disorder was added in 2004, and depression in bipolar disorder was added in 2009. Also added in 2009 were marketing indications in ages 13-17 for pediatric schizophrenia (based upon one 6 week RTC[89(C-1)]) and pediatric manic or mixed episodes in bipolar I disorder (based upon one 3 week RCT[90(C-3)]). At that time, clinicians noted the propensity of olanzapine to cause weight gain and increase blood lipids in the pediatric population.

The ten-year literature review identified 9 RCTs of olanzapine: 3 addressed psychosis/schizophrenia, 1 studied bipolar disorder, 1 assessed treatment in pervasive developmental disorders (PDD), 2 compared olanzapine with clozapine (see analysis above), and 2 compared olanzapine with risperidone and haloperidone or molindone. Four POLs met criteria: 1 assessed olanzapine treatment in schizophrenia spectrum disorders, 1 looked at bipolar disorder treatment, and 2 addressed PDDs. (Eight other POLs compare olanzapine with one or more other antipsychotic medications. See Antipsychotic Comparisons section and Table I.) Figure 2 below summarizes these trials and provides Table C references.

Figure 2
Olanzapine Clinical Trials Summary

Olanzapine Trial Population	Tot #	Ages	RCT Study references Numbers refer to Table C	POL Study references Numbers refer to Table C
Disruptive behaviors (DB)				
Autism Spectrum (PDD)	3	6-17	4	6,9
Schizophrenia spectrum	2	13-17	1	7
SCZ prodrome	2	12-17	2,5	
Bipolar disorders	2	5-17	3	8
Tic disorders				

From the RCTs, olanzapine was found more effective than placebo in ages 13 and up for treating pediatric schizophrenia[89] and bipolar mania.[90] These RCTs are the basis of the FDA approval for marketing. Efficacy in PDDs is equivocal.[91] For youth at risk of developing schizophrenia, olanzapine is not effective at delaying the onset of psychosis.[92] It has no role to play in treating cognitive function in this group as contrary to previous thinking, this group displays no deterioration in function prior to onset of psychosis.[93] Open label studies suggest that effectiveness in schizophrenia maintains for at least a year and extends down to age 6.[17] In bipolar disorder effectiveness likely extends down to age 5 and further includes depressive, psychotic, and aggressive symptoms.

Summary Olanzapine has FDA marketing indications for schizophrenia, bipolar mania and bipolar mixed episodes for ages 13 and up. The literature suggests further effectiveness down to age 4 in bipolar disorder and age 9 in schizophrenia. Use of olanzapine in delaying the first onset of psychosis is not supported. It is unclear if olanzapine is helpful in pervasive developmental disorders (autism spectrum disorders). Olanzapine is equivalent to risperidone, quetiapine, and haloperidol in psychotic disorders but appears to cause more weight gain and higher blood lipid levels. It might be more effective than other antipsychotics against the negative symptoms of schizophrenia or in patients with refractory schizophrenia.[50] (See Antipsychotic Comparison Section and Table I.)

Quetiapine (Table D)

Quetiapine (QTP) is a second generation antipsychotic medication first approved for marketing in 1997, making it the fourth medication available in this group. Initial marketing approval was for treatment of psychosis in adults, and marketing indications for monotherapy and adjunctive therapy of acute mania in bipolar I disorder were added in 2004. Treatment of major depressive episodes associated with bipolar disorder was added as a marketing indication in 2006, while maintenance treatment as an adjunct to lithium or divalproex was added in 2008. Finally in 2009 marketing indications for pediatric schizophenia (ages 13-17) and pediatric bipolar disorder (ages 10-17) were approved on the basis of 1 RCT each.

The ten-year literature search identified 5 papers describing results in 4 RCTs and 3 papers describing 3 POLs that met criteria for review. These papers do not include those mentioned above that formed the basis for the FDA pediatric marketing approval. Those papers appear to have not yet been published at the time of this review. Five other papers addressed trials that compared two or more antipsychotic medications. (See Antipsychotics Comparison section and Table I.) Figure 3 below summarizes those few clinical trial papers meeting review criteria that have been published and references them to Table D.

Figure 3
Quetiapine Clinical Trials Summary

Quetiapine Trial Study Population	Tot #	Ages	RCT Study references Numbers refer to Table D	POL Study references Numbers refer to Table D
Bipolar Disorder (BD)				
Mania in BD	2	12-18	4, 5	
Depression in BD	1	12-18	1	
Mood symptoms, high risk for BD	1	12-18		8
Schizophrenia spectrum	1	12-17		6
Disruptive behavior disorders				
Disruption behavior disorder + ADHD	1	12-16		7
Conduct Disorder	1	12-17	2	
Disruptive behaviors and BD	1	12-18	3	

Quetiapine was not more effective than placebo for treating depression in bipolar disorder[94] although one POL suggested it might be effective for mood symptoms in adolescents at high risk for bipolar disorder.[95] (These adolescents do not have bipolar disease but are at high risk for developing the disease due to having close family members with the disease.) Quetiapine was as effective as divalproex for mania [Q16] and disruptive behaviors occurring in bipolar I disorder.[96] Addition of quetiapine to divalproex was more effective than divalporex alone.[97] In addition it appeared faster-acting. [98]

One POL echoed the unpublished FDA study as it suggested that quetiapine is effective in schizophrenia spectrum disorders.[99] One other suggested it is helpful for severe aggression when added to methylphenidate in attention deficit/hyperactivity disorder (ADHD).[100] One final RCT showed that although it was effective for some symptoms in conduct disorder, it was not effective for aggression in these patients.[101] Weight gain was a problem in the longer studies, especially when no stimulant such as methyphenidate was also being used.

Summary Quetiapine has few published pediatric studies and what few have been done have not been replicated. It is approved by the FDA for marketing for the indications of pediatric bipolar disorder and schizophrenia. It is further effective as an adjunctive treatment in mania. Quetiapine does not appear effective for treatment of depression in bipolar disorder and its use for aggression alone appears equivocal. Weight gain is a problem but less so in patients receiving a concurrent stimulant.

Ziprasidone (Table E)

Ziprasidone (ZIP) was FDA approved for marketing in 2001 for the indication of adult schizophrenia, making it the fifth second generation antipsychotic available in the U.S. Manic and mixed episodes in bipolar I disorder in adults were added in 2004 and its use as an adjunct in maintenance bipolar treatment was added in 2009. There are no FDA approved pediatric marketing indications at this time.

The ten-year literature search reveals very few published papers for ziprasidone that met review criteria. Early concerns about cardiac side effects are likely to have made it an unpopular choice for pediatric clinical trials in the few years it has been available. Two ziprasidone POLs were identified as well as one comparison POL between aripiprazole and ziprasidone. No RCTs were identified between June 1, 2000 and May 31, 2010. There is one published pilot RCT from earlier in 2000 that will be included in this review because there is so little evidence otherwise. Papers are summarized in Figure 4 below with reference to Table E.

Figure 4
Ziprasidone Clinical Trials Summary

Ziprasidone Trial Study Population	Tot #	Ages	RCT Study references Numbers refer to Table E	POL Study references Numbers refer to Table E
Mixed disorders				
Mania, schizophrenia, schizoaffective	1	10-17		2
Tourettes, OCD, or PDD	1	7-18		3
Tourette's Disorder*	1	7-17	1*	

*Out of review period; included to expand evidence.

Ziprasidone appeared to be effective in the one treatment POL[26] for manic and schizophrenia/schizoaffective symptoms, but has some limitations as shown in the second POL that studied ECG changes.[32] This study noted that some pre-existing cardiac conditions and the concurrent use of drugs that affect electrical conduction in the heart can limit the use of ziprasidone and that clinicians can not rely on the use of automated ECG readings to ascertain risk and follow changes due to lack of accuracy in this area. The one RCT from early in 2000 found ziprasidone to be effective treatment for tics.[102] In the comparison POL, ziprasidone and aripiprazole were found to be equally effective in the treatment of severe aggression across a variety of diagnoses. Generally studies noted that ziprasidone is much less likely to cause weight gain and EPS than other second generation antipsychotics.

Summary Ziprasidone has no pediatric FDA marketing indications, few clinical trials, and a general paucity of evidence to support its use. Evidence suggests that it is effective for tics, mania, schizophrenia, and schizoaffective disorder, and that it causes less weight gain and EPS. Unfortunately cardiac monitoring is required for its use, to include a pediatric cardiologist reading of ECGs, and patients must be carefully assessed for pre-existing cardiac disease and the concurrent use of other medications affecting cardiac function. One recent systematic literature review of ziprasidone concludes: "Given the dearth of randomized controlled trials with ziprasidone, its use in children and adolescents should only be considered a second or third-line option at best, for limited indications."[103, p. 226]

Aripiprazole (Table F)

Aripiprazole (ARI) is a second generation or atypical antipsychotic first approved for marketing by the FDA in 2002 for schizophrenia in adult patients. Manic and mixed bipolar episodes in adults were added as indications in 2004. In 2007, based on one 6-week placebo controlled trial, schizophrenia in adolescent patients aged 13-17 years was added as a new indication. The age range for use was extended again in 2008 to include ages 10-17 based upon one 4-week placebo controlled trial that addressed the indication of bipolar mania in adolescents. Finally in 2009, treatment of irritability associated with autistic disorder in pediatric patients aged 6 to 17 year was added as a new indication based upon two 8-week placebo controlled trials.[104,105]

The ten-year literature search identified 6 papers describing results in 5 RCTs and 4 POLs that met criteria for review. These papers included those mentioned above that formed the basis for FDA marketing approval and that were funded by industry. (One final paper described a POL that compared aripiprazole with ziprasidone. See Antipsychotic Comparisons section and Table I.) One RCT addressed schizophrenia, two

addressed disruptive behaviors in autism, and two addressed bipolar disorder. The POLs studied: tic disorders-one study, aggression in conduct disorder—one study, and autism spectrum—one study. Figure 5 summarizes these clinical trials and references them to Table F.

Figure 5
Aripiprazole Clinical Trials Summary

Risperidone Trial Population	Tot #	Ages	RCT Study references Numbers refer to Table F	POL Study references Numbers refer to Table F
Disruptive behaviors (DB)	1	13-17		7
Autism Spectrum	3	5-17	2*,3*	8
Schizophrenia spectrum	1	13-17	6*	
Bipolar disorders	2	8-17	4*,5	
Tic disorders	2	7-17		9

*Studies that led to FDA approval for pediatric marketing indications

Aripiprazole was found to be more effective than placebo in treating symptoms of schizophrenia in ages 13-17 years,[29] manic and mixed episodes associated with bipolar disorder in ages 10-17 years,[106,107] and irritability in autism in ages 6-17 years.[104,105] It was not effective for depression associated with bipolar disorder in one trial.[106] Open label studies suggested that aripiprazole may be effective for aggression in conduct disorder[108] and for tics in tic disorders.[25] When appropriately dosed, aripiprazole was well tolerated in all clinical trials up to 36 months. Weight gain occurred over 36 months in the longest trial, but the pattern and amount was not analyzed further nor compared to normal growth expected in childhood.[108] (The final open label study suggested that aripiprazole and ziprasidone were equally and highly effective for aggression in a population of children age 6-18 years with many different diagnoses.[24] See Antipsychotic Comparison Section and Table I.)

Summary Aripiprazole has FDA marketing indications for acute treatment of patients with pediatric schizophrenia, bipolar disorder, and autism in patients as young as age 6. The literature suggests effectiveness for aggression and tics, but for these symptoms, it should be reserved for those patients who have failed to respond to medications that have more clearly established efficacy or for those who are unable to take other medications because of their side effect profile. Long-term maintenance on aripiprazole up to three years appears well tolerated and suggests that chronic treatment for the range of disorders may be appropriate.

Paliperidone (Table G)

Paliperidone (PAL) was approved for marketing for adult schizophrenia in 2006, making it the seventh atypical or second generation antipsychotic available in the U.S. It has since been approved in 2009 for further marketing for mono- and adjunctive therapy in adult schizoaffective disorder. PAL is an active metabolite of risperidone. In the body, risperidone is transformed by the liver into paliperidone, which acts on receptors in the brain as do all other antipsychotics. It has been suggested for those patients who have impaired liver function. These persons cannot take risperidone due to the potential inability to metabolize it well with loss of efficacy and possible resultant toxicity. Paliperidone has no FDA pediatric marketing indications and the ten-year literature search turned up no clinical trials that addressed the use of this medication in children. Because paliperidone is a metabolite of risperidone, its presence in children who have

been treated with risperidone is discussed in studies related to that drug. However, safety and efficacy of direct administration of this medication in children is not documented by appropriate studies at this time.

Iloperidone (Table G)

Iloperidone was FDA approved in 2009 for marketing for the treatment of schizophrenia in adults. It has no pediatric indications approved for marketing at this time. The literature search identified no published pediatric studies or papers. This medication is the eighth atypical or second generation antipsychotic on the market. It can slow electrical conduction in the heart and cause blood pressure problems similar to ziprasidone and consequently even in adults must be used with extra caution. Due to the lack of any published pediatric studies of any sort, the use of iloperidone in children and adolescents is not supported at this time.

Asenapine (Table G)

Asenapine is the newest second generation antipsychotic to come on the market in the U.S. The FDA has approved its marketing for adult schizophrenia and mixed/manic episodes in adult bipolar I disorder. It has not been approved for marketing for pediatric indications at this time. The ten year literature search does not identify any papers relating to the use of this medication in pediatric patients. Due to the lack of any published pediatric studies, the use of asenapine in children and adolescents is not supported at this time.

PEDIATRIC TRIALS FOR FIRST GENERATION ANTIPSYCHOTICS

First Generation Antipsychotics (Table H)

There are a number of first generation antipsychotic medications currently on the market and in the Texas Medicaid Vendor Drug Program: chlorpromazine, haloperidol, molindone, perphenazine, pimozide, thioridazine, thiothixene, fluphenazine, and trifluoperizine. (It should be noted that molindone was discontinued by the manufacturer in 2010 and is not expected to be available after June 30, 2010.) These medications as a group have been little used in recent years for children and adolescents with psychiatric problems. Although used previously in child psychiatry, the volume of patients seen in previous decades was far less than today and antipsychotic medications in general were used far less. Long hospitalizations were more common then for serious psychiatric and behavioral disorders.

There have been no clinical trials with FGAs in the last ten years except the rare comparison study. Very few clinical trials of these medications exist, even dating back 40 years, that would meet criteria for this review. Because of their historical importance, chlorpromazine and haloperidol are described separately in this section. Table I summarizes the antipsychotic comparison clinical trials.

Chlorpromazine (Table H)

Chlorpromazine was first approved for marketing in 1955 for emesis (vomiting) and later in 1957 was the first medication available in the U.S. approved for an antipsychotic marketing indication.[109] Complete FDA marketing indications from the package insert are:

> For the management of manifestations of psychotic disorders.
> For the treatment of schizophrenia.
> To control nausea and vomiting.
> For relief of restlessness and apprehension before surgery.
> For acute intermittent porphyria.
> As an adjunct in the treatment of tetanus.
> To control the manifestations of the manic type of manic-depressive illness.
> For relief of intractable hiccups.
> For the treatment of severe behavioral problems in children (1 to 12 years of age) marked by combativeness and/or explosive hyperexcitable behavior (out of proportion to immediate provocations), and in the short-term treatment of hyperactive children who show excessive motor activity with accompanying conduct disorders consisting of some or all of the following symptoms: impulsivity, difficulty sustaining attention, aggressivity, mood lability and poor frustration tolerance.[110]

All versions of the original Thorazine brand product are now discontinued and no longer available. It became available as a generic drug in 1973 and is only available as a generic today. The ten-year literature search reveals that chlorpromazine is not being actively studied in pediatric psychiatry at this time. Abstracts of papers published in this area in the 1960s and 1970s are not available through PubMed. The first obvious controlled clinical trial (as opposed to a review or description) appears in 1972. Studies in the early years centered on its use in hyperactivity, "disturbed subnormal patients," "disturbed children" including preschoolers, preschool schizophrenia, and childhood schizophrenia. In the 1980s, papers addressing its use in preventing nausea and vomiting appear along with its use as a pre-anesthetic or for conscious sedation for children undergoing painful procedures. These types of papers continue into the 1990s. Chlorpromazine is used infrequently in psychiatry today because it is very sedating and more frequently causes constipation, dry mouth, urinary retention, and blurry vision. It can cause tardive dyskinesia, although less so than other FGAs. Other FGAs such as haloperidol have a higher incidence of tardive dyskinesia. However today, chlorpromazine remains a very effective anti-nausea medication for single or limited use and has come full circle to its beginnings. Current prescription for children and adolescents in psychiatric care is limited and the evidence base is not current and very thin despite a long history of use.

Haloperidol (Table H)

Haloperidol was approved for marketing in 1967 for adult schizophrenia. Later, pediatric indications for ages 3 and up were added:

> Haloperidol is indicated for use in the management of manifestations of psychotic disorders. Haloperidol is indicated for the control of tics and vocal utterances of Tourette's Disorder in children and adults. Haloperidol is effective for the treatment of severe behavior problems in children of combative, explosive hyperexcitability (which cannot be accounted for by immediate provocation). Haloperidol is also effective in the short-term treatment of hyperactive children who show excessive motor activity with accompanying conduct disorders consisting of some or all of the following symptoms: impulsivity, difficulty sustaining attention, aggressivity, mood lability, and poor frustration tolerance. Haloperidol should be reserved for these two groups of children only after failure to respond to psychotherapy or medications other than antipsychotics.[111]

Patient profile from STAR Health psychotropic medication utilization review process

Case#5: 12-year old male with ADHD, combined type and severe impulsive aggression. This youth has had multiple suspensions from school and psychiatric hospitalization for physical aggression. He has assaulted and severely injured peers by attacking them without provocation. He has also assaulted teachers and destroyed property. He is treated with medications for ADHD, which help with focus and concentration, and he is doing well academically when he decides to do his work. He is frequently irritable, and others are afraid of him. He will yell out inappropriate comments in class and is highly disruptive. The antipsychotic medication quetiapine was added to his medication regimen twice a day, and his impulsive aggression has improved. The school was considering either expelling him or putting him in a self-contained classroom. Based on his improvement, he may be able to remain in his regular class.

This youth has severe ADHD and the stimulant medications have resulted in improvement of only part of his ADHD symptoms. He remains irritable, and has significant impulsive aggression that is causing severe consequences at school. The use of antipsychotics in this case is off label but warranted due to the symptom severity. Antipsychotic medication can have multiple actions - it can reduce impulsivity, aggression, and act as a mood stabilizer. Not using an antipsychotic medication could result in this child being prescribed three or four other medications that have a higher risk profile than the antipsychotic medications.

Four clinical trials were identified in the ten year literature search, two RCTs and two POLs. These are all comparison studies and are described in the separate Antipsychotic Comparison Section. Please see that section for important information supporting the summary below. Although not strictly a psychiatric indication, haloperidol was modestly effective as a sleeping agent for pediatric burn patients in one RCT.[112]

Summary Haloperidol has wide FDA marketing indications for ages 3 and up: psychotics disorders, Tourette's disorder, severe behavior problems (combative, explosive hyperexcitability), and hyperactivity with impulsivity, inattention, aggression, mood lability, and/or poor frustration tolerance. It is noted to only be appropriate for use in severe behavior problems and hyperactivity when psychotherapy or medications other than antipsychotics have failed to ameliorate the problem. Although modestly effective as a sleeping agent in children with severe medical issues, other more commonly used medications should be tried first. Please see section below for evidence from the

antipsychotic comparison studies.

COMPARISON OF SGAs TO EACH OTHER AND FGAs

Antipsychotic Comparison Studies (Table I)

The ten-year literature search identified 18 papers that compared two or more antipsychotic medications. There are a few other papers already discussed in the sections on individual medications that compared an antipsychotic medication with a medication from a different class. These are not discussed in this section. Risperidone, compared in 15 of the 19 papers, is again the most studied antipsychotic drug in pediatric comparison trials just as it was in the other clinical studies. Figure 6 below summaries the types of comparison studies and references Table I.

Figure 6
Comparison Clinical Trials Summary

Comparison studies	Tot #	Ages	RCTs	POLs	Comments Target of studies
RIS vs OLZ	3			1,2,6	2 - prolactin study
RIS vs QTP	1			14	Cardiac safety study
RIS vs QTP vs OLZ	4			4,5,8(retrospective),11	2 in SCZ, 2 any dx
RIS vs OLZ vs MOL	1	8-17	3		Schizophreniform
RIS vs OLZ vs HAL	2		9	18	Psychosis
RIS vs HAL	2		15	16	Autism
RIS vs PIM	1		17		Tics
CLZ vs OLZ	3		7,10	12	Schizophrenia
ARI vs ZPS	1		13		Aggression

POL comparison studies suggest risperidone and olanzapine are both effective and equally so in childhood schizophrenia down to age 9[113] and bipolar mania in ages four to six years.[114] Both appear to increase prolactin levels, risperidone > olanzapine, early on, though at the end of one year levels are similar.[115] Both seem unimpressive in treating disruptive behaviors in the 4-6 year old group.[114] Further, these uncontrolled studies suggest that risperidone might be better at treating depression in bipolar disorder[114] and olanzapine, in line with its relation to clozapine, might be better at treating negative symptoms, such as a reduction of emotional unresponsiveness, motivation, socialization, speech and movement.[113] The POL comparing risperidone with quetiapine for first onset psychosis suggested that risperidone was slightly more clinically effective than quetiapine though statistically it was not.[116] (This study outcome may be more meaningful because it was funded by the maker of quetiapine.)

POL studies comparing two second generation antipsychotics, olanzapine and quetiapine (QTP), with risperidone suggested they are all equally effective for schizophrenia spectrum disorders.[12,117] The medications appeared to differ only in their propensity to cause increased weight (olanzapine, risperidone > quetiapine), increased blood lipids (olanzapine, quetiapine > risperidone), and increased prolactin levels (risperidone > olanzapine, quetiapine).[118,28]

Two studies funded by the maker or risperidone, one RCT and one POL, compared risperidone with haloperidol. These concluded that risperidone was superior to haloperidol for acute and maintenance treatment in autism.[14,15] In RCT comparison studies down to age 8, second generation antipsychotics, risperidone and olanzapine, were equivalent in efficacy to first generation antipsychotics, molindone (MOL)[12] and haloperidol (HAL)[13], for childhood psychotic disorders. These medications only differed in the side effects associated with them. Olanzapine and risperidone appeared to cause more weight gain

than molindone and haloperidol (olanzapine > risperidone > haloperidol > molindone). Molindone and haloperidol appeared to cause more movement disorders, especially akathisia.[13] The one POL with older children had the same result.[119] Risperidone was superior to pimozide for tic disorders in another RCT although it produced more weight gain.[120]

Overall, olanzapine is equivalent to risperidone, quetiapine, and haloperidol in psychotic disorders but appears to cause more weight gain and higher blood lipid levels. It might be more effective than other antipsychotics against the negative symptoms of schizophrenia or in patients with refractory schizophrenia.[50]

Superiority of clozapine to olanzapine was not demonstrated except for treatment of negative symptoms in those children who were considered treatment resistant.[50] (In the RCT from 1996, clozapine was clearly superior to haloperidol for both positive and negative symptoms in refractory pediatric schizophrenia.[53])

The final open label study suggested that aripiprazole and ziprasidone were equally and highly effective for aggression in a population of children age 6-18 years with many different diagnoses.[24]

Summary The available pediatric comparison studies are not large enough to conclusively settle which of the antipsychotics are most effective. A larger study would be required to do this. However, the available comparison studies generally show that when compared, first and second generation antipsychotics have equivalent efficacy in the disorders typically treated by this class of medication: schizophrenia spectrum disorders, bipolar disorders, tic disorders, autism spectrum disorders, and disruptive behaviors. However, all the medications have not been compared with one another for the total range of disorders. Differences between the medications appear to reside almost exclusively in the side effects produced.

Evidence for Use in the Very Young

As can be seen from Figure 7 below, the youngest age for FDA marketing approval of any SGA is 5 years for risperidone in treating autism. Several FGAs are much lower—as young as 6 months for chlorpromazine. Although the FDA has approved this marketing, it is not based on the rigorous RCTs now required for all new medications. Several clinical trials have studied children as young as 2 years old with autism and found safety and some efficacy for risperidone for up to six months.[71,73] Other studies that included very young children tended to not have a large proportion in that age group and most times did not analyze data for them separately from older children.[60,86,77] When this analysis did occur, the studies tended to show less response in those very young children.[71,76]

The Preschool Psychopharmacology Working Group reviewed all the literature in this area and published guidelines in 2007 for use of these medications in a variety of disorders seen in this age group.[121] Risperidone is recommended for use in pervasive developmental disorders (autism spectrum disorders) with severe aggression. A high level of evidence supports this recommendation. At the next level of evidence, risperidone was recommended before mood stabilizers in preschool bipolar disorder with emotional dysregulation. Finally, risperidone, at the lowest level of evidentiary confidence, was recommended for severe and persistent impairing disruptive behaviors for children who failed to respond to multiple other treatment interventions.

While there are few high quality clinical trials on the use of antipsychotics in very young children, risperidone is the antipsychotic that has been studied the most in children and adolescents. It is the antipsychotic most frequently cited in the review of the Preschool Psychopharmacology Working Group because there is more positive data for it than any other. However, although a search of the PubMed database for "risperidone" in youth turns up hundreds of citations, only a small fraction of these papers represent high quality clinical trials, and only a very few of these provide useful information for very young children. Concern about use of any antipsychotic in preschool children appears warranted because there is so little known about effects on very young children or their later brain development.

Sources of Bias in the Evidence Base

The pharmaceutical companies design, conduct and pay for the marketing studies, then apply for FDA marketing approval, and ultimately financially profit from drugs on the market. Until encouraged by the FDA with a financial incentive of a 6-month extension of exclusive marketing, only a few pharmaceutical companies pursued safety and efficacy clinical trials for psychoactive medications in youth. Out of the 95 studies resulting in 100 papers described in this review, at least 31 were funded by the National Institute of Mental Health (NIMH), the National Institutes of Health (NIH), or another governmental, academic, or nonprofit entity. Six of these 31 appeared to have at least some further funding from industry. Some papers did not describe a funding source. The pharmaceutical industry frequently supplied study medications even for clinical trials it did not directly fund. For each study listed in Tables A-I, the first column includes a description of the funding source.

Trials funded by theoretically unbiased sources do not appear to differ substantially from industry funded ones except in size. Industry funded clinical trials tend to be much larger and therefore much more expensive to conduct. Industry does not generally publish trials that have negative results. Although the failure to publish negative results likely happens in general academic funded scientific research, it is probably less common in academic drug research because negative results are perceived as very important in this area. There would be no academic or personal disincentive in studies funded by non-profit entities. In spite of this, very few papers in this review describe results in which the drugs were not effective.

One relatively negative paper that did not show a robust treatment effect for risperidone in 2.5-6 year olds was funded by industry.[122] Another study with only minimal positive results listed no funding source and is likely not funded by industry.[71] An astonishing example from the antipsychotic comparison clinical trials concluded one antipsychotic was better than another even though there was no statistically significant difference—a negative outcome for the other drug. In this case the study was funded by the maker of the other drug![116]

Bias exists in the pharmaceutical industry sponsored clinical trials on the basis of this sample of studies and is likely to be pervasive in our culture and so large as to be difficult to detect.

Patient profile from STAR Health psychotropic medication utilization review process

Case #6: 13-year old female with major depression, and post traumatic stress disorder (PTSD) who continues to have anxiety, hypervigilence, irritability, depression, frequent flashbacks and nightmares. She has had multiple psychiatric hospitalizations for suicidal thoughts and cutting on her arms and stomach. She has been treated with medications for depression, but continues to have episodes of irritability and anxiety. She also has unwanted thoughts of her stepfather molesting her and beating her when she asked him to stop having sex with her. She does not want to go to sleep at night because she is afraid of having nightmares where she is beaten and locked in a closet. The antipsychotic medication ziprasidone was added to her medication regimen, and after 3-4 days she is starting to not avoid sleep, she is less anxious, and her irritability is improving. She is also starting to have fewer flashbacks and nightmares.

Psychological problems and psychiatric symptoms include anxiety, depression, mood instability, symptoms of PTSD (hypervigilence, flashbacks, and nightmares) and self abusive behavior. Her most prominent symptoms are PTSD symptoms, and the use of antipsychotics is off label in this case but warranted due to the symptom severity. The antipsychotic medication can have multiple actions - it can reduce anxiety, depression, and intrusive thoughts and act as a mood stabilizer. Not using an antipsychotic medication could result in this child being prescribed three or four other medications which have a higher risk profile than the antipsychotic medications.

Summary of FDA Marketing Approval and Clinical Trial Evidence Base

Figure 7 below summarizes which antipsychotics have FDA marketing indications and further clinical trial evidence in the five main clinical categories in which they are prescribed. The "literature supported" category indicates medications that have substantial RCT evidence that extends the FDA marketing age range or provides a clinical indication not included at all in the FDA marketing indication. The "literature suggested" category indicates there are POL studies or smaller, shorter RCTs that suggest clinical efficacy and safety for the listed medication. No high quality clinical trial evidence exists for the use of multiple concomitant antipsychotics, and none for the use of antipsychotics in preschool (under age 5) children except in autism spectrum disorders. No high quality clinical trial data exists regarding use for longer than three years.

Figure 7
Indications for Antipsychotic Use by FDA and Evidence Base Status

Condition	FDA Approved Marketing	Literature Supported Large, multiple, and/or large effect size RCAs	Literature Suggested Small, short, or smaller effect size RCAs, POLs
Schizophrenia	Risperidone 13-17 Olanzapine 13-17 Quetiapine 13-17 Aripiprazole 13-17 *Haloperidol** 3+ *Thioridazine*** Peds *Trifluoperazine*** 6+		Clozapine: In the treatment resistant Olanzapine 6-15 Quetiapine 12-17 Ziprasidone 10-17
Bipolar mania or mixed episodes	Risperidone 10-17 Olanzapine 13-17 Quetiapine 10-17 Aripiprazole 10-17	Risperidone: 4-17: For adjunctive treatment Aripiprazole 8-17	Olanzapine 5-14 Quetiapine 12-17: prodromal mood symptoms Ziprasidone 10-17
Autism - PDDs	Risperidone 5-16 Aripiprazole 6-17	Risperidone 2-17	Olanzapine 6-17
Tic disorders	*Haloperidol ** 3+ *Pimozide*** 2+		Risperidone 7-17 Ziprasidone 7-17 Aripiprazole 7-17
Disruptive behavior/aggression	*Chlorpromazine** 6mos + *Haloperidol** 3+	Risperidone 5-17	Quetiapine 12-17 Aripiprazole 13-17:

*FDA approval does not have strong RCT support; few to no clinical trials in last 10 years
**No FDA approval, but labeling implies some FDA support because advice on use in pediatric age group (Peds) is given
First generation antipsychotics or typicals are listed in italics.

Evidence Applied to Clinical Practice

Process of Evaluation and Treatment

Prior to prescription, clinicians must assess the child or adolescent. A complete evaluation consists of the history of the symptoms bringing the patient to the doctor, the child's physical, social, and emotional development, previous diseases and treatment, illnesses in the family, and a review of any other symptoms present. Finally, the clinician performs a mental status examination. A mental status exam consists of a series of questions that assesses awareness, thought processes, memory, sensory perceptions, emotional state, insight, judgment, personality, and behavior. The examiner notes not only the content of the answers, but also observes behavior elicited by the questions in the setting of the exam.

Unfortunately, there are no laboratory tests or measurements that can definitively diagnose psychiatric disorders. Clinicians diagnose with the combination of the typical description of symptoms, historical factors, and mental status exam findings.

Psychological testing may be used, but it is expensive and generally not necessary unless confounding factors or treatment failure warrants it.

Once the diagnosis is made, clinicians select appropriate treatment based upon the training, experience, current scientific information, available resources, characteristics of the patient, and preferences of the youth and parents or guardians. The clinician considers the severity of the symptoms, the age and size of the youth, response to prior medications and previous treatments, other health conditions present, other ongoing treatment, and the patient's susceptibility to adverse effects of any proposed medication. Risks and benefits of treatment are discussed with the child and the responsible adult and agreement or consent to begin treatment is obtained.

Consent to Treatment

Consent to treatment is not a single act in time, but rather a discussion and process that is ongoing in the treatment relationship between the clinician, the parent or guardian, and the youth. The consent process requires that the clinician describe the:

1. Nature of the illness being treated
2. Proposed treatment
3. Expected benefits and possible risks including side effects
4. Other treatments that may be available and why the clinician recommends the proposed treatment ahead of them
5. Consequences of not undergoing the treatment

Additionally, the clinician should offer to answer questions and work to accommodate the preferences of the responsible adult and youth when eliciting consent.

Strictly speaking, youth under age 16 cannot give legal consent to mental health treatment in Texas. Instead clinicians seek consent from the responsible adult and assent from the child for any treatment proposed. This entails explaining the treatment at a developmentally appropriate level, answering questions, and securing the youth's agreement to try the treatment.

In Texas, formal consent is required in the Texas Administrative Code for treatment with psychoactive medications in psychiatric hospitals[123] and for treatment of foster care youth.[124] Psychiatric hospital settings are frequently locked and medications are administered by a nurse. The formalized consent process in hospitals assures the rights of individuals and/or their guardians to refuse treatment and minimizes the possibility of coercion. In the foster care setting, formal consent protects the rights of minors who are under the care of the state.

In regular outpatient settings, the process is somewhat less formal. In this setting the patient or responsible adult is presumably administering the medication and can withdraw consent at any time simply by stopping the medication. Although less formal, the items that should be described and discussed are still the same and the prudent clinician documents this process carefully as expected by ethical professional standard.

Selection of Treatment

With the exception of aggression/disruptive behaviors, the conditions for which antipsychotics are commonly prescribed are not presently considered curable, although recovery is possible. These disorders, schizophrenia, bipolar disorder, autism, and tic disorders are continuous with ones that occur in adulthood that are also treated with antipsychotic medication. Schizophrenia and bipolar disease more commonly appear in very late adolescence and adulthood, while autism, tic disorders, and disruptive behavior disorders typically begin in childhood. Schizophrenia and bipolar disease that do appear in childhood generally are more severe and have a worse prognosis than the same illnesses when first appearing later in life.

In schizophrenia, bipolar disorder, and tic disorders, antipsychotics are used to treat the primary symptoms of the disorders: psychosis, mania, and tics respectively. In autism and disruptive behavior disorders, these medications are mainly used to treat associated symptoms of irritability and impulsiveness, which can lead to aggression and dangerous risk-taking. The effect on irritability and impulsiveness is also helpful in ameliorating the agitation and aggression that can be found in other disorders.

Schizophrenia and psychosis

Antipsychotic medication is the mainstay of appropriate treatment for schizophrenia. Prior to the introduction of these medications treatment was very difficult and the prognosis for recovery was poor. Other psychosocial treatments are also used but are secondary to appropriate medication management. Although not widely studied in other conditions that have psychosis as a feature, antipsychotics are the only known effective medication for hallucinations and delusions. Therefore, these medications are frequently recommended and may be the only rapidly effective treatment available when psychosis is present. The current standard of care, professional guidelines, and current research literature all support the use of antipsychotics to treat schizophrenia in youth and adults. Wide clinical consensus exists for their use in any psychosis.

Bipolar mania and related conditions

In bipolar disorder, mood stabilizers are frequently used first. If psychotic, manic, or irritability/impulsivity symptoms remain or are prominent that interfere with functioning at home, school, or community, then antipsychotics are used. Other treatments such as supportive psychotherapy augment medication in these two illnesses to support the youth in managing the illness during daily life. Both schizophrenia and bipolar disorder have strong genetic components and can be shown to have biochemical and structural brain changes. The current standard of care, professional guidelines, and current research literature support the use of antipsychotics to treat bipolar disorder in youth and adults.

Autism and autism spectrum disorders

In autism, no medication has been found that reliably treats the developmental and social deficits that define the disorder. Environmental intervention and skills training in areas

of the deficits are the most effective measures known so far. Medications such as antidepressants may be used to address anxiety and obsessive-compulsive features while antipsychotics are used to address irritability and aggression that frequently accompany autism. Not every youth will need medication for these associated features. However, when obsessive behavior and irritability are present in severe forms, treating these symptoms can make it possible for the youth to participate in the other treatments.

Autism is also recognized as a brain disorder that appears to exist as a continuum from mild forms such as Asperger's disorder to classical autism. It has strong genetic components and can be shown to have structural brain changes. Milder forms do not usually exhibit the extreme irritability which can lead to severe aggression that is seen in the classical form. It may be appropriate to treat severe irritability in milder forms if other treatment approaches have failed and the youth's home and school functioning are thereby impaired. The current standard of care, professional guidelines, and current research literature support the use of antipsychotics to treat irritability autism in youth and adults.

Tic Disorders

Tic disorders in mild forms commonly occur in childhood. Many times they do not require treatment. Tourette's disorder is a severe form that manifests with muscle and/or vocal tics. It mildly or extremely disrupts normal functioning. When severe, antipsychotic medications suppress the tics and allow a normal life. Tic disorders are recognized to be disorders of the brain. The current standard of care, professional guidelines, and current research literature support the use of antipsychotics for severe impairing tics in youth and adults.

Disruptive Behavior and Aggression

Disruptive behavior disorders are a group of conditions that are frequently associated with irritability, impulsivity, and aggression. Attention deficit hyperactivity disorder, oppositional defiant disorder, conduct disorder, and intermittent explosive disorder are frequently classed in this group. Generally treating each of these with environmental intervention, behavior modification, and psychotherapies precedes using medications of any class. When aggression is severe and risk of harm to self or others high, medication may be used sooner.

The use of antipsychotics for aggression is perhaps the most controversial with the lay public, although there is quality data showing efficacy for treatment of aggression that has not responded to other measures. A meta-analysis of the nine clinical trials that reported on antipsychotic effect in aggression found a mean effect size (ES, Cohen's *d*) of 0.9 for risperidone.[125] Effect size is a statistical calculation (0.0 to 1.0) that allows comparison of treatment effects across different studies with different methodologies. Any effect size greater than 0.4 is considered clinically significant because these changes are not only statistically significant, but also clinically easily observable. The 0.9 mean effect size of risperidone on aggression reported in this meta-analysis is very large.

The addition of antipsychotic medication to psychosocial interventions, such as parent management training, frequently produces better results with a lower medication dose, than either intervention singly.[126] The current standard of care, professional guidelines, and current research literature support the use of antipsychotics to treat severe aggression unresponsive or insufficiently responsive to other measures in youth and adults.

Choice of when to prescribe and which antipsychotic

The choice of when to use an antipsychotic depends upon the diagnosis, severity of the symptoms, risk to the youth and others of not using an antipsychotic, the availability of other effective evidence-based treatments, and the resources of the community and family to support treatment. A physician's judgment regarding the efficacy of any medication for any patient will take into account a number of criteria, such as symptoms, age and weight, other medications being taken by the patient, whether the patient has successfully taken a medication previously, the patient susceptibility to or experience of side effects over time, whether the patient is receiving other behavioral services, and the patient's reaction to a medication observed through monitoring. Treatment guidelines for most disorders generally recommend using medications after psychosocial interventions have been shown to be insufficiently effective. Schizophrenia and bipolar disorder are the possible exceptions, but these youth generally do not receive these diagnoses until considerable time has passed since the onset of symptoms. In this time many other interventions have usually occurred.

Parents, daycares, schools, foster homes, and other institutions pressure clinicians when severe disruptive behavior occurs. This can make it difficult to try appropriate psychosocial interventions first or for a sufficient time for them to be effective. This type of pressure particularly occurs when institutions threaten to expulse youth because of their behavior.

The choice of which antipsychotic to use in each of these disorders for a specific individual child will vary according to differences in FDA marketing approval status, specific clinical effectiveness and side/adverse effect profile as reflected in the clinical trial evidence base, and the clinical characteristics and needs of the youth and family in question. For example, an underweight child with a past history of encephalitis and seizures in addition to their bipolar disorder would be considered for olanzapine because olanzapine has strong evidence of effectiveness, appetite stimulation, and lessened propensity to cause neurological side effects in a child already neurologically compromised. A very obese youth with a history of heart defect, severe intractable aggression and oppositional defiant disorder would likely fare better on aripiprazole, an SGA with lowered risk of increased appetite and weight gain and some literature support of effectiveness in aggression.

VI - Antipsychotic Medication Use in Texas Medicaid Youth

As noted in the Introduction, since 2007 Texas has participated in a collaborative multi-state project to examine the use of antipsychotic medications for children and adolescents in Medicaid. This project was sponsored by the Medicaid Medical Directors Learning Network and the Agency for Healthcare Research and Quality (AHRQ)-funded Rutgers Center for Education and Research on Mental Health Therapeutics (CERT). The work Texas HHSC, DFPS, and DSHS sponsored in 2005 and 2006 to produce the *Texas Psychotropic Medication Utilization Parameters for Foster Children* (Texas Parameters) and analyze data on the use of psychoactive medication in Medicaid children in foster care occupied a prominent place in this project. Many of the methods used in Texas to extract and define the use of claims data to produce meaningful information about prescription of psychoactive medications informed the methods used across the country in this project. The Texas Parameters dose guidelines were adopted by the project for use in data analysis for all 16 states.

In June 2010, this group released, "Antipsychotic Medication Use in Medicaid Children and Adolescents: Report and Resource Guide From a 16-State Study."[127] (See Appendix H.) The 16 states that participated in the study did so voluntarily and likely are some of the more active states in addressing concerns about psychiatric care. This report has detailed information on methodology used to produce mental health drug utilization reports from pharmacy claims systems, a compendium of practices used by the 16 states related to antipsychotic utilization review, and an overview of analyses of the pooled results from these states. Each state also received an individual report that showed how it compared to others in aggregate. State-by-state comparison data was not made public as differences between the ways individual states collected and maintained claims data was felt to lead to erroneous conclusions. (See Appendix C for Texas results.)

Across the 16 states studies, the report shows that prescribing of psychoactive medication to children in foster care is much more common than prescribing to other Medicaid children, which reflects the fact that many youth in foster care have complex behavioral health care conditions and they also may be dealing with the trauma of difficult family situations and being removed from their families.

The report for Texas shows that from 2004 to 2007 (the period covered by the report) rates of use of antipsychotics in Medicaid children age 18 years and younger is below the mean for the 16 states in the study. These rates, however, rose over that time period by 16 percent in this broad Medicaid population. This is in contrast to rates in Texas children in foster care, which dropped by 10.5 percent during the same time period. Use of antipsychotics in the subpopulation of Medicaid children aged 5 and younger is higher than the 16 state mean, but dropped 14 percent from 2004 to 2007. Children in foster care as a whole were prescribed more antipsychotics than the 16 state average in spite of the downward trend. These data show that while overall Texas Medicaid physicians prescribed fewer antipsychotic medications than the average, they did tend to use more antipsychotics with younger age groups and children in foster care.

On other measures, Texas began the study period as the state showing the highest proportion of high dose antipsychotic use in 2004 (based upon dosages used in the Texas Parameters). This rate declined by 57 percent during the study period to just above the mean for the 16 states. Texas began the study period above the mean in use of multiple antipsychotics, but after a 19 percent drop, ended the study period in 2007 below the 16 state mean. Use of multiple mental health drugs (apart from multiple antipsychotic medications) was also above the mean in Texas although it dropped 12 percent over the study period. Texas showed maximum rates of use of multiple mental health drugs in youth in foster care, although these did drop 19 percent by 2007. This drop still placed Texas as the state with the highest use of multiple mental health drugs in this population.

Recent analysis by HHSC shows that antipsychotic prescribing to Texas Medicaid youth has continued to increase for the Medicaid pediatric population. The percent of youth under age 16 receiving an antipsychotic medication for ≥ 60 days grew about 18 percent from 2007 to 2009 (from 0.7 percent to 0.8 percent). The percent of Medicaid children under age 6 who were prescribed an antipsychotic medication for ≥ 60 days grew almost 20 percent from 2007 to 2009 (from 0.15 percent to 0.19 percent).

Although prescribing levels are substantially higher for children in foster care, antipsychotic prescribing to this population in Texas continued to decline from 2007 to 2009. Of children under age 16 enrolled in STAR Health, the managed care program for children in foster care, antipsychotic prescribing for ≥ 60 days decreased about 4.5 percent from 2007 to 2009, and prescribing to children under age 6 decreased about 23 percent during that same time period. A more detailed analysis of prescribing trends for all psychoactive medications (including antipsychotics, antidepressants, stimulants and mood stabilizers) to children in foster care is described below.

Texas' Medicaid foster care population has received intense scrutiny and intervention since 2005. Following the release of the Texas Parameters in February 2005, DFPS, HHSC and DSHS took many steps to encourage appropriate prescribing of psychoactive medications to children in foster care. DFPS and HHSC widely distributed the parameters to medical providers, Child Protective Services (CPS) staff, judges and residential care providers, with targeted communication to the highest volume prescribers and those with most patients falling outside the guidelines. HHSC, DFPS and DSHS periodically update the parameters to reflect the most current clinical information on these medications (See Appendix A).

In April 2008, HHSC in close collaboration with DFPS implemented the STAR Health statewide managed health care system for Medicaid youth in foster care. STAR Health includes a medical home model, electronic health passport, and a utilization review system based on the Texas Parameters to monitor clinical psychiatric prescribing. See Appendix F for a more detailed description of the Psychotropic Medication Utilization Review (PMUR) process for STAR Health enrollees, which uses eight criteria to review individual client cases based on the Texas Parameters.

Patient profile from STAR Health psychotropic medication utilization review process

15-year old male with schizophrenia and obsessive compulsive disorder (OCD) who has a history of irritability, fear of others, anxiety, and bizarre behaviors. He has repeatedly cut up his clothes and smeared feces on the wall in his bedroom. He is withdrawn, and isolates himself to his room. In his room, he will place objects around the room in patterns and when his mother tries to clean his room he becomes agitated and aggressive. This has resulted in multiple psychiatric hospitalizations for bizarre behavior and danger to others. He has been treated with medications for depression, mood instability, and both older and second generation antipsychotics. The last antipsychotic medication he was on was quetiapinel at 800mg/day and he was not aggressive but he was very sleepy and would fall asleep at school. The quetiapine dose was reduced to 600mg/day and low dose haloperidol 2 mg at night was added to his medication regimen.

Psychological problems and psychiatric symptoms include anxiety, paranoid ideation, mood instability, and symptoms of OCD, and impulsive aggressive behavior. The use of quetiapine as an antipsychotic and mood stabilizer is FDA approved for schizophrenia in this age group; however, the dose needed to control most of the symptoms caused significant sedation. The use of two antipsychotics is off label, but warranted due to the symptom severity. Antipsychotic medication can have multiple actions - it can reduce anxiety, psychosis, intrusive thoughts, act as a mood stabilizer and reduce aggression.

Since 2005 and likely as a consequence of these changes, prescribing of psychoactive medications in the foster care population has been on a downward trend. Rates of prescribing of psychoactive medications to this population are down in every category tracked by HHSC and DFPS. Based on data analyzed by HHSC, the percentage of foster youth receiving any psychoactive medication for ≥ 60 days peaked in state fiscal year 2004 at 29.9 percent and at the end of state fiscal year 2009 had dropped to 19.7 percent. The rate of youth in foster care who experienced class polypharmacy has dropped by nearly 75 percent, and the percentage receiving 5 or more psychoactive medications is down by nearly 80 percent. These drops are attributed in large part to use of the Texas Parameters as audit flags for utilization review in the health system developed for this group. (See the Update on the Use of Psychoactive Medications in Texas Foster Children Fiscal Years 2002-2009 in Appendix B.)

Clearly, the trend toward decreasing rates in Texas for antipsychotic use in Medicaid youth for most measures described above is encouraging. However, while antipsychotic prescribing rates in the general Medicaid children's population are much lower than rates in the foster care population, overall prescribing of antipsychotics in the general population continues to increase. It is felt that the difference in overall trend between the general Medicaid children's population and the foster care population is largely due to the utilization review system in place for the latter subpopulation. The downward trend in high dose use and use of multiple medications in the general population may also be due to the release of the Texas Parameters and utilization review in the foster care population. Although the guidelines and the utilization review system specifically target the foster care population, there is some overlap between the physicians treating youth in foster care and those treating the general Medicaid youth population.

VII - Discussion

The peer-reviewed scientific literature provides the only current, readily available and reliable, safety and efficacy data for the use of antipsychotic medications in children and adolescents. This literature documents short and intermediate term safety and efficacy of many antipsychotic medications in a number of pediatric behavioral health conditions. This literature shows that antipsychotics have efficacy in the same disorders in youth as they do in adults with one exception—they have not shown efficacy in youth depression. They show the same side effects and adverse effects although probably at higher rates. Evidence from adult trials of all psychoactive medications has actually been fairly accurate at predicting response in youth trials except for depression.

The rising use of antipsychotic medications in youth, especially very young children, is problematic. Little to no data exists for use of any of these medications in children under age 3 for any condition and little to no reliable data exists on the concurrent use of multiple antipsychotic medications. There is no current way to assess for rare effects and the long-term effects (as in decades later) of these medications on the developing brain.

Although some categories of the use of antipsychotics in youth in Texas are declining, the overall proportion of use in the Medicaid pediatric population is still rising. Use of this class of medications for aggression and bipolar disorder is the most common and the most controversial.

Aggression can be a component of a wide variety of behavioral disorders. It is non-specific and easily gets the attention of caregivers, schools, and the community because of the risk to the youth and others around him or her. Aggression is seldom a primary symptom in a disorder. Because it can accompany almost any disorder, the diagnosis on a claim form may not at first appear to be one for which an antipsychotic is appropriate. Aggressive behavior may arise due to a complex combination of biological and environmental factors. Understanding the underpinnings of aggression in any individual child requires careful assessment. All clinical guidelines and research on aggression are unequivocal in the recommendation for careful assessment and the use of psychosocial interventions ahead of medication whenever possible. These interventions can be time and labor intensive.

Bipolar disorder was not even widely recognized as a pediatric disorder until the 1990s. Its diagnosis remains controversial even in psychiatric circles, although most clinicians do conclude youth can suffer from the disorder. Many feel it is over diagnosed, however. Careful assessment distinguishes it from other disorders, especially in the very young. When confirmed, medication treatment, including antipsychotic medications, is considered primary treatment because the disorder is unlikely to respond to psychosocial treatments alone.

Recent research in adults has shown that the older antipsychotics, the first generation, are as effective as the much more expensive second generation medications. Growing literature in youth verifies the same finding. Many policy makers have questioned the

almost exclusive use of the SGAs on this basis. Formularies and health systems may push for the use of FGAs through step therapy policies, which require one drug or class of drug to be tried before another drug or class. Sometimes they are referred to as "fail first" policies. The patient must first fail to respond to one drug before the other drug may be prescribed.

There is comparatively little to no high quality clinical trials of FGAs in this population—especially in the last ten years. Consideration should be given before moving from expensive, relatively well-studied medications to ones that are cheaper, but with much less high quality evidence in the pediatric population. Consideration also should be given to side effect profiles and the clinical needs of the patient.

Some groups have proposed that prior authorization be required for the prescribing of antipsychotics to children below a certain age. HHSC has a current prior authorization program related to the Medicaid preferred drug list and for specific clinical edits. HHSC utilizes two advisory bodies of physicians and pharmacists – the Pharmaceutical and Therapeutics Committee (P&T Committee) and the Drug Use Review Board (DUR Board) – to advise HHSC on the development of the preferred drug list, clinical edits, and prior authorization criteria.

Under the current prior authorization program, if HHSC cannot determine through its automated systems whether the client meets prior authorization criteria for a particular medication, the physician's office must seek prior authorization through a phone call before the pharmacy may dispense the prescription to the patient. This system adds to the cost of providing care on the provider side due to the time and extra labor involved and also is an administrative cost to Medicaid. In the case of prior authorization associated with the Medicaid preferred drug list and clinical edits, HHSC's goal is to encourage the prescribing of safe, efficacious and cost effective medications. HHSC solicits input from providers and other Medicaid stakeholders on prior authorization criteria and has worked with the provider community to reduce the administrative hassle of the prior authorization process.

One recent study in Georgia showed that PA for second generation antipsychotics lowered costs and improved care.[128] A similar study in Georgia and Mississippi using data from the mid-1990s, however, had the opposite result. Decreased pharmacy costs were associated with increased outpatient services costs for schizophrenic patients.[129]

In the Texas Medicaid program, payment rates to providers of behavioral health are considered to be low compared to both Medicare and private insurance plans. Adding extra costs for providers may drive some out of the program, thereby decreasing access to care. There already exists a shortage of psychiatrists and other behavioral health practitioners in Texas. (See Appendix E) Prior authorization may create a barrier to appropriate use of medications. Primary care physicians may choose to avoid treating behavioral health problems and specialty providers may drop out the program or never enter it. A study of PA for SGAs in Maine showed that although PA did decrease the rates of initiation of SGA therapy, there was no corresponding increase in rates of other

therapy in this chronically mentally ill population.[130] This was interpreted to mean that PA had created a barrier to appropriate treatment even though providers did not drop out.

Whatever measures are taken to provide support and guidance to Medicaid providers and youth recipients around the issue of appropriate use of antipsychotics, the role of parents needs consideration. For the general Medicaid youth population, the child's parent or guardian is well positioned to understand the needs of the individual child and weigh the risks and benefits of any given treatment—including off-label medication use. When making treatment decisions, this population deserves high quality information about the full range of treatments and access to the widest possible range of evidence-based treatment interventions.

Caveats on the Use of Claims Data to Shape Public Policy

The use of financial claims data to draw conclusions about clinical practice in a given population has limitations. Texas' Medicaid claims data consists of two very large data sets, pharmacy claims and encounter claims. Pharmacy claims are generated when a prescription is filled by a patient and contains basic identification and demographic data on the patient, identification of the pharmacy/pharmacist, the drug, dose, amount dispensed, and cost. It identifies the prescriber by a code that corresponds to a prescriber database. Pharmacy claims do not contain diagnostic information. Encounter claims contain basic identification and demographic data for the patient, identification of provider using an identification code system, procedure code, and diagnosis code(s), and cost.

Correlating these two databases has limitations because no direct connections exist between a pharmacy claim in one database and the patient encounter claim in the other that produced the prescription. Indeed, the patient encounter may not have even produced a claim to Medicaid. Some providers never file encounter claims, some encounters occur under conditions that Medicaid will not pay (e.g. phone calls), and some encounters are with non-Medicaid providers. Sometimes a patient has seen a clinician multiple times in a short time frame, or has seen multiple providers. Which pharmacy claim goes with which encounter claim? Although the prescriber for the pharmacy claim is known, he or she may be initiating or continuing a medication at the request of the patient or another clinician that recently saw the patient. The diagnosis in effect may get lost on the claim form. Many pediatricians believe that a mental health diagnosis on a claim form will lead to denial of the claim and therefore omit these diagnoses. In any case, matching a pharmacy claim with a corresponding diagnosis from an encounter claim creates problems.

Claims data also reflects that antipsychotics' original purpose was to sedate for procedures. They have other properties that make them useful in non-psychiatric conditions. Many of the FGAs have anti-nausea and anti-histamine properties. Promethazine is a phenothiazine (same chemical class as chlorpromazine) that has been marketed for many years for allergy symptoms, nausea, vomiting, and sedation for procedures. Because of these other properties, antipsychotics are sometimes prescribed for other uses. This can be seen in the pediatric neurologist's office, ambulatory surgical

centers, and hospital intensive care units. The ability of these medications to stimulate appetite and cause weight gain can also be useful in debilitated individuals who fail to eat because of lack of appetite. Diagnoses from claims data that match to pharmacy claims may be readily available but misinterpreted to mean inappropriate prescription for psychiatric care.

Many difficulties present when using claims data to draw conclusions about clinical practice. In aggregate, with appropriate methodology and an understanding of the considerable limitations, claims data can provide meaningful information about large trends and the effects of system interventions. To understand what is actually happening in clinical encounters or with individual patients or prescribers requires a much different approach.

Limitations of This Report

This report has several limitations that should be kept in mind when policy makers consider antipsychotic medication use in the Medicaid youth population. No new analyses of Texas data have been done. This report relies on data and analyses already available. It provides a primarily descriptive, not analytical, review of the current situation as documented in professional research literature and state, federal, and national public information.

While HHSC sought to do as comprehensive a literature review as possible for this report, the clinical trial literature base collected is undoubtedly incomplete. Additional submitted papers filled in some gaps but many times did not meet inclusion criteria. Because of the relative homogeneity of findings in similar studies, papers missed would be unlikely to present radically different information. In any case, no attempt was made to perform a scientific meta-analysis of the research literature reviewed. A comprehensive critical meta-analysis of this same research literature base is due to be published later this or early next year.[131]

This report does not address the very important issues of appropriate assessment and other treatments available for youth behavioral health problems. Stakeholders submitted many papers, articles, and even books on these topics, but these areas were beyond the scope of work for this project. Time and resource constraints limited this report to the central topic of use of antipsychotics in youth. It is recognized generally by all the cited practice guidelines that appropriate assessment is the first step in treatment of any problem. All guidelines mentioned psychosocial interventions as important first steps in some cases and as concurrent treatment the vast majority of the time. Where appropriate, this report notes these principles.

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Table A

Second Generation Antipsychotics (Atypical)

Clozapine

Study & Funding source	Met criteria	Safety	Efficacy	Conclusions, Limitations, Comments
Clozapine Generic available Clozaril® Fazaclo® 5 PubMed citations, June 2,2010 Search terms: clinical trials [PT] AND clozapine AND (child OR adolescent) NOT adult	RCTs: 0 POLs: 1 (More in Table I Antipsychotic Comparisons: 2 RCTs & 1 POL)	Adverse Events: Hypersalivation Sedation Weight gain Metabolic abnormalities Cardiovascular side effects Seizures Agranulocytosis Serious side effects limit the use of CZP in adults. Children may develop these side effects at greater rates than adults.	No FDA marketing indications in pediatric patients. In adults, FDA marketing indications in treatment-resistant schizophrenia & recurrent suicidal behavior in schizophrenia or schizoaffective disorders. Uniquely effective in treatment refractory childhood onsent schizophrenia (COS). [CLZ0]	"Clozapine remains the most effective medication for treatment refractory cases of COS both for short-term and maintenance treatment." [CLZ0 p. 463] "...clozapine should still be a third-line medication in children reserved for treatment-refractory cases" [CLZ0 p. 463] Clozapine is the gold standard for effectiveness in schizophrenia in adults as it is clearly superior to other antipsychotics. The risk of adverse effects however is large compared to other antipsychotics.
Kranzler H, Roofeh D, Gerbino-Rosen G, Dombrowski C, McMeniman M, DeThomas C, Frederickson A, Nusser L, Bienstock MD, Fisch GS, Kumra S. Clozapine: its impact on aggressive behavior among children and adolescents with schizophrenia. J Am Acad Child Adolesc Psychiatry. 2005 Jan;44(1):55-63. PMID: 15608544 Funding Source: NIMH; NARSAD; NSLIJ Research Institute General Clinical Research Center	POL 24 wks 20 pts 8.5-18 yrs Schizophrenia with aggression	Not assessed in this study.	Decrease in use of oral emergency medication: -0.16 events/d p = 0.000 Decrease in use of injectable emergency medication: -0.03 events/d p = 0.007 Decrease in use of seclusion: -0.03 events/d p = 0.003	"The present data suggest that in children and adolescents with schizophrenia, clozapine may diminish violence and aggression and may hasten discharge to a less restrictive setting." [no page numbers] Limitations: lack of control group, no randomization, open label, use of other meds

Table B

Second Generation Antipsychotics (Atypical)

Risperidone

Study & Funding source	Studies that met criteria	Safety	Efficacy	Conclusions Limitations Comments
Risperidone (RIS) Generic available Risperdal® 86 PubMed citations, June 2, 2010 Search terms: clinical trial [PT] AND risperidone AND (child OR adolescent) NOT adult	RCT's: 22 + 3 RCT post hoc papers POL's: 21	Common Adverse effects sedation increased appetite headache nausea/vomiting weight gain increased prolactin levels EPS	FDA Marketing Indications: Irritability in autism, acute and maintenance, 5-16 schizophrenia 13-17 bipolar I 10-17 RCT data shows efficacy for disruptive behaviors including aggression.	Oldest SGA except for clozapine. Most studied antipsychotic in youth probably because it has been on market longer in new era of increased clinical trials in youth. Longest study is 3 years Youngest age studied: 2 yrs
Pandina GJ, Zhu Y, Cornblatt B. Cognitive function with long-term risperidone in children and adolescents with disruptive behavior disorder. J Child Adolesc Psychopharmacol. 2009 Dec;19(6):749-56. PMID: 20035593 Funding Source: Johnson and Johnson Pharmaceutical Research and Development.	RCT 6 mos 284 pts 5-17 Disruptive Behavior Disorder	Adverse Events somnolence 2% overall 3 in risperidone group 3 in placebo group Other AE's not assessed	MVLT-C learning trial total ≥ 0.5 SD improvement RIS: 30.37% PBO: 31.58% CPT "Easy" version pr ≥0.5 SD improvement RIS: 26.77% PBO: 28.24% SD = Standard deviation MVLT-C = modified California Verbal Learning Test for Children CPT = Continuous Performance Test	With both cognitive assessment measures, patients were more likely to improve than worsen; this was true regardless of treatment condition." p. 754 "Risperidone treatment resulted in no decline in cognitive function among children and adolescents." p. 749 Limitations: low and narrow dose range, risperidone non-responders not included, no normal control, fewer placebo condition completers, full range of cognitive function not assessed Comment: Results may not hold for higher doses of risperidone.
Haas M, Unis AS, Armenteros J, Copenhaver MD, Quiroz JA, Kushner SF. A 6-week, randomized, double-blind, placebo-controlled study of the efficacy and safety of risperidone in adolescents with schizophrenia. J Child Adolesc Psychopharmacol. 2009 Dec;19(6):611-21. PMID: 20035579 Funding Source: J&J Pharmaceutical Research and Development. Study used in FDA approval process.	RCT 6 wks 160 pts 13-17 yrs SCZ	Adverse Events RIS 1-3 mg: 75% RIS 4-6 mg: 76% PBO: 54% Serious AE's: RIS 1-3 mg: 2% Ris 4-6 mg: 2% PBO: 4% Most related to underlying psychiatric disorder EPS increases compared to baseline (but all changes small) RIS 1-3: 33% RIS 4-6: 39% PBO: 15% Wt gain: RIS 1-3 mg: +1.3 kg RIS 4-6 mg: +1.5 kg PBO: +0.12 kg Difference between RIS groups not significant. Prolactin: no related clinical AE's seen although serum levels increased in treatment groups Cardiac & other lab: no clinically meaningful changes	PANSS change RIS 1-3 mg: -21.3 RIS 4-6 mg: -21.2 PBO: -8.9 RIS (both gps) vs P: p < 0.001 Responded (≥20% reduction in PANSS total score): RIS 1-3 mg: 65% RIS 4-6 mg: 72% PBO: 35% PANSS = Positive and Negative Symptom Scale	"Risperidone 1-3 mg/day and 4-5 mg/day were well tolerated and effective in adolescents experiencing acute episodes of schizophrenia. The benefit-risk profile suggests that a dose of 1-3 mg/day might be optimal for this population." p. 611 Limitations: fixed dose study, forced titration to maximally tolerated doses with in the 2 dose ranges, short length Comment: The forced titration may have increased the number of AE's over what would be seen in clinical practice.

Table B

Second Generation Antipsychotics (Atypical)

Risperidone

Study & Funding source	Studies that met criteria	Safety	Efficacy	Conclusions Limitations Comments
Haas M, Delbello MP, Pandina G, Kushner S, Van Hove I, Augustyns I, Quiroz J, Kusumakar V. Risperidone for the treatment of acute mania in children and adolescents with bipolar disorder: a randomized, double-blind, placebo-controlled study. Bipolar Disord. 2009 Nov;11(7):687-700. PMID: 19839994 Funding Source: Johnson & Johnson Pharmaceutical Research ad Development Study used in FDA approval process.	RCT 3 wks 169 pts 10-17 yrs Manic or mixed episodes in Bipolar Disorder	Most common Adverse Events: somnolence headache fatigue Serious AE's: RIS 0.5-2.5 mg: 6% RIS 3-6 mg: 8% PBO: 5% Most related to underlying psychiatric disorder. Wt gain: RIS 0.5-2.5 mg: 1.9 kg RIS 3-6 mg: 1.4 kg PBO: 0.7 EPS (AIMS score change) RIS 0.5-2.5 mg: -0.02 RIS 3-6 mg: -0.08 PBO: +0.11 Differences are not statistically significant.	YMRS change: RIS 0.5-2.5 mg: -18.5 RIS 3-6 mg: -16.5 PBO: -9.1 Responders (≥50% reduction on YMRS): RIS: 0.5-2.5 mg: 59% RIS: 3-6 mg: 63% PBO: 26% YMRS = Young Mania Rating Scale	"At daily doses of 0.5-2.5 mg and 3-6 mg, risperidone was effective and well tolerated in children and adolescents experiencing acute manic or mixed episodes of bipolar I disorder. Results indicate that risperidon 0.5-2.5 mg has a better benefit-risk profile than risperidone 3-6 mg." p.687 Limitations: short length, forced titration to max dose within groups; participants had co-morbid disorders—most commonly a disruptive behavior disorder Comment: Forced titration within dosage group may have increased the number of AE's over what would be seen in clinical practice. Patients treated with risperidone experienced a slight decrease in AIM's scores which reflects improvement in involuntary movements over placebo which evidenced a slight increase or worsening. This may reflect EPS from previous treatment being uncovered by placebo while being "masked" by further treatment with an antipsychotic—a well-known phenomenon. In any case the magnitude of all these differences is so small as to be statistically insignificant.
Aman MG, Hollway JA, Leone S, Masty J, Lindsay R, Nash P, Arnold LE. Effects of risperidone on cognitive-motor performance and motor movements in chronically medicated children. Res Dev Disabil. 2009 Mar-Apr;30(2):386-96. Epub 2008 Sep 2. PMID: 18768293 Funding SourceJanssen Pharmaceutic supplied study medications. Other funding not documented in paper.	RCT 2 wks + 2wks 16 pts 4-14 yrs Disruptive Behavior IQ ≤ 84	AIMS No significant difference between RIS and placebo. RIS caused weight gain compared to placebo. p = 0.02 AIMS = Abnormal involuntary Movement Scale	Cognitive motor tests showing drug effect (all are clinically positive effects) Task — p STRM response time — 0.01 STRM Seat movements — 0.05 GHT Contacts — 0.05 No other tests showed significant effects positive or negative. STRM = Short Term Recognition Memory GHT = Graduated Holes Task	"The findings suggest a beneficial effect of risperidone after several months of treatment on efficiency of responding, activity level, static tremor, and aspects of behavior." p. 396 Limitations: diagnostic heterogeneity, small sample size, less control over community portion of sample Comments: Consistent with other studies, this one showed a lack of effect on the Contiuous Performance Task. Risperidone did not seem to affect memory.
Aman MG, Hollway JA, McDougle CJ, Scahill L, Tierney E, McCracken JT, Arnold LE, Vitiello B, Ritz L, Gavaletz A, Cronin P, Swiezy N, Wheeler C, Koenig K, Ghuman JK, Posey DJ. Cognitive effects of risperidone in children with autism and irritable behavior. J Child Adolesc Psychopharmacol. 2008 Jun;18(3):227-36. PMID: 18582177 Funding Source: NIMH	RCT 8 wks 38 5-17 Autism and severe behavioral disturbance	AE's other than those related to cognition not assessed in this study.	Perdue Pegboard and Analog Classroom Task: no significant differences between treatment conditions. RIS > PBO on Cancellation Task and Verbal Learning Task. No decline in performance seen with risperidone.	"Risperidone given to children with autism at doses up to 3.5 mg for up to 8 weeks appears to have no detrimental effect on cognitive performance." p. 227 Limitations: no statistical correction for multiple comparisons, small sample size, only those older and/or with higher IQ's able to perform tests in study, Comment: Persons with autism are very difficult to assess for cognitive measures.

Table B

Second Generation Antipsychotics (Atypical)

Risperidone

Study & Funding source	Studies that met criteria	Safety	Efficacy	Conclusions Limitations Comments
Armenteros JL, Lewis JE, Davalos M. Risperidone augmentation for treatment-resistant aggression in attention-deficit/hyperactivity disorder: a placebo-controlled pilot study. J Am Acad Child Adolesc Psychiatry. 2007 May;46(5):558-65. PMID: 17450046 Funding Source: Janssen, LP.	RCT 4 wks 25 pts 7-12 yrs Treatment resistant aggression in ADHD	Rates of Adverse Events did not differ significantly between RIS and PBO. AE's > 10%: Abdominal pain Vomiting No clinically significant changes were found in weight gain, hematology, blood chemistries, or vital signs.	Responders (≥30% improvement on CAS-P) RIS: 100% PBO: 77% No differences found on CAS-T CAS-P = Childrens' Aggression Scale-Parent CAS-T = Children's Aggression Scale-Teacher	"Risperidone treatment appears to be well tolerated and modestly effective when used in combination with psychostimulants for treatment-resistant aggression in children with ADHD." p. 558 Limitations: small sample size, short length, no control for type and dose of concomitant stimulant medication Comments: Pilot study is not definitive only suggestive. This study had a very large placebo response.
Lindsay RL, Eugene Arnold L, Aman MG, Vitiello B, Posey DJ, McDougle CJ, Scahill L, Pachler M, McCracken JT, Tierney E, Bozzolo D. Dietary status and impact of risperidone on nutritional balance in children with autism: a pilot study. J Intellect Dev Disabil. 2006 Dec;31(4):204-9. PMID: 17178532 Funding Source: NIMH, NIH; Janssen Pharmaceutica donated study medications.	RCT + POL 2 mos + 4 mos 20 pts + 8 pts 5-13 yrs Autism	Baseline: Overall nutrient intake exceeded RDI. Deficiencies (< 80% RDI) for individuals in: Calcium: 9/20 pts Pantothenic acid: 6/20 pts Vit D: 5/20 Vit K: 8/20 2 Months: Wt increased, Vit K intake increased with RIS treatment 4 Months: No significant changes Wt. gain: RIS: +3.7 kg PBO: +1.6 kg Age/gender corrected BMI z scores reflected that weight increase was significant.	Efficacy not assessed.	"These pilot data suggest that treatment with risperidone did not significantly affect the nutritional balance of this small group of children." p. 204 Limitations: small sample size, study relied on parent report Comment: This study reflects the imbalance in nutrient intake and increase in food intake seen in mental health patients even prior to medication treatment.
Luby J, Mrakotsky C, Stalets MM, Belden A, Heffelfinger A, Williams M, Spitznagel E. Risperidone in preschool children with autistic spectrum disorders: an investigation of safety and efficacy. J Child Adolesc Psychopharmacol. 2006 Oct;16(5):575-87. PMID: 17069546 Funding Source: Janssen Pharmaceutica	RCT 6 mos 23 pts 2.5-6.0 yrs Autism Spectrum Disorders	No serious Adverse Events No EPS Common AE's: Transient sedation (both RIS & PBO) Increased appetite (both RIS & PBO) One subject on PBO withdrew due to increased hyperactivity Wt. gain: RIS: +2.96 kg PBO: +0.61 kg p = 0.008 Prolactin levels: RIS: +33.38 ng/ml PBO: +11.11 ng/ml p = 0.015	Childhood Autism Rating Scale change RIS: -4.6 PBO: -1.8 p = 0.114	"Study findings suggest that risperidone is well tolerated in preschoolers over a 6-month period, but that only minimally greater improvement in target symptoms was evident in the risperidone group, possibly due to the differences between groups at baseline or due to the small sample size." p. 575 Limitations: small sample size, all children received Applied Behavioral Analysis; although randomized, children in RIS group had significantly greater severity of symptoms on CARS at baseline; although all raters were blinded to treatment condition, the treating psychiatrist was not blinded Comments: As in most studies of autism, the medication did not affect the core social symptoms in this disorder, but only the disruptive behaviors.

Table B

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Study & Funding source	Studies that met criteria	Safety	Efficacy	Conclusions Limitations Comments
Pandina GJ, Bossie CA, Youssef E, Zhu Y, Dunbar F. Risperidone improves behavioral symptoms in children with autism in a randomized, double-blind, placebo-controlled trial. J Autism Dev Disord. 2007 Feb;37(2):367-73. PMID: 17019624 Funding Source: All authors are employees of Janssen related companies.	RCT 8 wks 55 pts 5-12 yrs Autism	Most common Adverse Event: Somnolence RIS: 74% PBO: 7%	Aberrant Behavior Checklist-Irritability subscale change: RIS: -13.4 PBO: -7.2 P < 0.05 ES =-0.7	"Risperidone treatment was well tolerated and significantly improved behavioral problems associated with autism." p. 367 Limitations: short length, small sample size, no long term assessment
Nagaraj R, Singhi P, Malhi P. Risperidone in children with autism: randomized, placebo-controlled, double-blind study. J Child Neurol. 2006 Jun;21(6):450-5. PMID: 16948927 Funding Source: Department of Pediatrics, Postgraduate Institute of Medical Education and Research, Chandigarh, India; Sun Pharmaceuticals supplied study medications.	RCT 6 mos 40 pts 2-9 yrs Autism	Adverse Events: Increased appetite Sedation: 20% (mild) Transient dyskinesias: 3 pts 1 pt on PBO lost to follow-up Weight gain: RIS: 2.81 kg PBO: 1.71 kg Difference not statistically significant	Response on CARS (≥20% over baseline): RIS: 63% PBO: 0% p < 0.001 Response on CGAS (≥20% over baseline): RIS: 89% PBO: 10% p = 0.035 CARS = Childhood Autism Rating Scale CGAS = Children's Global Assessment Scale	"Risperidone improved global functioning and social responsiveness while reducing hyperactivity and aggression inchildren with autism and was well tolerated." p. 450 Limitations: small sample size, fixed dose Comment: Contrary to most studies in autism, this one apparently shows a medication effect on a core symptom of social deficit.
Biederman J, Mick E, Faraone SV, Wozniak J, Spencer T, Pandina G. Risperidone for the treatment of affective symptoms in children with disruptive behavior disorder: a post hoc analysis of data from a 6-week, multicenter, randomized, double-blind, parallel-arm study. Clin Ther. 2006 May;28(5):794-800. PMID: 16861101 Funding Source: All authors have received research support from pharmaceutical companies, but paper does not document specific funding for this research.	RCT post-hoc analysis 6 wk 110 pts Mean age: ~8 yrs Disruptive Behavior Disorder	Not assessed in this study.	4 dimensional custom rating scale system derived from items of the Nisonger Child Behavior Rating Form: EI = Explosive irritability AEG = Agitated, expansive, grandiose Dep = Depression NAD = Nonaffective dimension Results at 6 wks (lower score is better) Scale / RIS / PBO / ES EI / 6.1 / 9.0 / 0.69 AEG / 7.0 / 8.1 / 0.44 Dep / 10.2 / 13.0 / 0.74 NAD / 13.8 / 23.8 / 0.95	"The results of this post hoc analysis of affective symptoms using data from a previously published double-blind, randomized clinical trial of risperidone versus placebo in the treatment of children with DBDs [disruptive behavior disorders] and subaverage intelligence suggest that risperdione was effective in treating the factors of explosive irritability; agitated, expansive, grandiose; and depression." p.794 Limitations: custom rating system, heterogeneous diagnoses and IQ levels, post hoc study Comment: RIS had greater effect compared to PBO on "nonaffective" conduct problems
Anderson GM, Scahill L, McCracken JT, McDougle CJ, Aman MG, Tierney E, Arnold LE, Martin A, Katsovich L, Posey DJ, Shah B, Vitiello B. Effects of short- and long-term risperidone treatment on prolactin levels in children with autism. Biol Psychiatry. 2007 Feb 15;61(4):545-50. Epub 2006 May 30. PMID: 16730335 Funding Source: NIMH; NIH	RCT + POL 8 wks + 4 mos 101 pts 5-17 yrs Autism	Prolactin levels not associated with any Adverse Events. Time / RIS / PBO / p Baseline / 9.3 / 9.3 / 8 wks / 39.0 / 10.1 / < .0001 6 mos / 32.4 / NA / < .0001 22 mos / 25.3 / NA / < .0001	Not assessed in this study.	"Risperidone treatment was associated with two- to four-fold mean increases in serum prolactin in children with autism. Limitations: blood samples not drawn fasting nor at standard times; long term risks of various levels are unknown at this time Comment: The prolactin levels decreased with time while RIS treatment continued.

Table B

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Study & Funding source	Studies that met criteria	Safety	Efficacy	Conclusions Limitations Comments
Reyes M, Buitelaar J, Toren P, Augustyns I, Eerdekens M. A randomized, double-blind, placebo-controlled study of risperidone maintenance treatment in children and adolescents with disruptive behavior disorders. Am J Psychiatry. 2006 Mar;163(3):402-10. PMID: 16513860 Funding Source: Johnson & Johnson Pharmaceutical Research and Development.	RCT 6 mos 335 pts 5-17 yrs Disruptive Behavior Disorders	Weight plateaued during this 6 month study after an initial increase in preceding 12 wks. Treatment discontinuation due to Adverse Effects: RIS: 1.7% PBO: 0.6% EPS: RIS: 3 pts PBO: 1 pt No tardive dyskinesia Prolactin: decreased in both RIS & PBO groups although at endpoint RIS group still ~2x higher. No clinically significant differences in cardiac parameters, lab other than prolactin, cognitive scores, or sexual maturation.	Time to symptom recurrence as measured by number of days until 25% of sample has sustained deterioration RIS 119 days PBO 37 days	"This study is the first placebo-controlled maintenance versus withdrawal trial of its kind in disruptive behavior disorder and provides evidence that patients who respond to initial treatment with risperidone would benefit from continuous treatment over the longer tem." p. 402 Limitations: Definition of symptom recurrence may be too conservative; possible selection bias Comment: As in other studies, over time, prolactin levels decrease towards baseline with continued RIS treatment.
Aman MG, Arnold LE, McDougle CJ, Vitiello B, Scahill L, Davies M, McCracken JT, Tierney E, Nash PL, Posey DJ, Chuang S, Martin A, Shah B, Gonzalez NM, Swiezy NB, Ritz L, Koenig K, McGough J, Ghuman JK, Lindsay RL. Acute and long-term safety and tolerability of risperidone in children with autism. J Child Adolesc Psychopharmacol. 2005 Dec;15(6):869-84. PMID: 16379507 Funding Source: NIMH; NIH; Janssen Pharmaceutica supplied study medications.	RCT + POL extension + RCT withdrawal phase 8 wks + 8 wks + 16 wks 101 pts (initially) 5-17 yrs Autism	Adverse Events: 3 pts discontinued RIS in acute trial 6 pts discontinues RIS in open-label extension Seizures in 2 pts (does not appear related to RIS) Lab: no clinically significant changes Weight gain: RIS: significant gains in both the RCT and open-label extension, but gain appeared to decelerate over time. Most common AE's: Adverse Event / PBO / RIS Tiredness 54% 94% Inc. appetite 38% 82% Nausea/vomiting 29% 41% Hypersalivation 16% 29% Dizziness 8% 22% Initial insomnia 65% 47% Anxiety 48% 32%	Efficacy not assessed in this study.	"All in all, tolerability was quite good in this study, shown by the fact that only 3 children (6.1%) discontinued risperidone in the acute trial and 6 subjects (9.5%) discontinued in the open-label extension because of AEs. This should be viewed in the context of very substantial reductions in volatile behavior with risperidone (RUPP Autism Network 2002). No unexpected AEs occurred, and the two instance of severe AEs (the 2 boys who had seizures) did not appear to be linked to risperidone." p. 882 Limitations: small sample size, short length Comments: This is a complex multi-part study with both RCT portions and open label portions. This study shows that sedation does decline with continued use as is often clinically asserted.

Table B

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Risperidone

Study & Funding source	Studies that met criteria	Safety	Efficacy	Conclusions Limitations Comments
Troost PW, Lahuis BE, Steenhuis MP, Ketelaars CE, Buitelaar JK, van Engeland H, Scahill L, Minderaa RB, Hoekstra PJ. Long-term effects of risperidone in children with autism spectrum disorders: a placebo discontinuation study. J Am Acad Child Adolesc Psychiatry. 2005 Nov;44(11):1137-44. PMID: 16239862 Funding Source: Korczak Foundation; Jannsen Cilag BV supplied study medications.	(POL) + RCT (8 wks + 16 wks) + 8 wks 24 pts 5-17 yrs Autism Spectrum Disorders	Most frequent side effects: Weight gain Increased appetite Anxiety Fatigue Weight gain: RIS: 5.7 kg at end of 24 wks of RIS treatment All Adverse Events in the mild to moderate range. EPS: no significant changes in AIMS or Simpson-Angus scores No withdrawal dyskinesias ECG, vital signs, lab: no clinically meaningful changes	Relapse over 8 wks: RIS: 3/12 25% PBO: 8/12 67% p = 0.049	"This study indicates the effectiveness of risperidone during a period of several months, reducing disruptive behavior in about half of the children with autism spectrum disorders. The results provide a rationale for the continuing use of risperidone beyond 6 months, although considerable weight gain can limit the use of this agent." p. 1137 Limitations: mean age of 9.0 yrs may make study less generalizable to adolescents, 90% male, high-functioning subjects, assessments performed by non-blinded assessors, long taper for RIS into PBO condition Comment: Complex study design.
LeBlanc JC, Binder CE, Armenteros JL, Aman MG, Wang JS, Hew H, Kusumakar V. Risperidone reduces aggression in boys with a disruptive behaviour disorder and below average intelligence quotient: analysis of two placebo-controlled randomized trials. Int Clin Psychopharmacol. 2005 Sep;20(5):275-83. PMID: 16096518 Funding Source: Janssen-Ortho Inc., Canada; Johnson & Johnson Pharmaceutical Research and Development.	"RCT" post hoc study of pooled data from 2 RCT's 6 wk 163 5-12 yrs Aggression in disruptive behavior disorders with subaverage intelligence	Not assessed in this study.	Aggression score (AS) = selected items from Nisonger Child Behavior Rating Form change: RIS: -5.7 (-54%) PBO: -2.3 (-21.7%) P < 0.0001 AS change P's for RIS compared to PBO for subsets: Pts with ADHD: P, 0.0001 Pts without ADHD: P = 0.052 Exact disruptive behavior diagnosis (CD or ODD) did not affect results.	"Risperidone was efficacious in reducing symptoms of aggression in boys of below average IQ with disruptive behaviour disorders." p. 275 Limitations: short length, small sample size, post hoc, comorbid ADHD allowed Comment: Risperidone effect was much greater for those with ADHD than those without ADHD.
Aman M, Buitelaar J, Smedt GD, Wapenaar R, Binder C. Pharmacotherapy of disruptive behavior and item changes on a standardized rating scale: pooled analysis of risperidone effects in children with subaverage IQ. J Child Adolesc Psychopharmacol. 2005 Apr;15(2):220-32. PMID: 15910206 Funding Source: Johnson & Johnson Pharmaceutical Research and Deveopment, Beerse, Belgium; Janssen-Ortho Inc., Toronto, Canada.	2 RCTs post hoc analysis 6 wks x 2 223 pts 5-15 yrs Disruptive behavior with subaverage IQ	Not assessed in this study.	Nisonger Child Behavior Rating Form Rating Scale/Subscale Items that Improved on RIS Subscale — Improved Items — ES Social Competence -Compliant/calm — 4/6 — 0.29-0.41 -Adaptive Social — 4/4 — 0.30-0.48 Problem Behavior -Insecure/anxious — 10/15 — 0.28-0.47 -Hyperactive — 5/9 — 0.38-0.44 -SIB/Stereotypyic — 1/7 — 0.21 -Self-isol./ritualistic — 3/8 — 0.22-0.29 -Overly sensitive — 1/5 — 0.52	"Beyond any effect on conduct problem symptoms, risperidone also appeard to improve aspects of social interaction, feelings of self worth, and reintegration.' p. 228 "Whereas most categories of problem behavior improved with risperidone, items reflecting "affective insecurity" and some infrequently endorsed items were unaffected in these children with DBDs and subaverage IQ." p. 220 Limitations: post hoc analysis Comment: "Risperidone is licensed for the treatment of DBDs in children, adolescents, and adults in several countries." p. 220 This paper did not report subscale total scores, p, or ES; it only reported mean scores for individual items in the N-CBRF along with p and ES.

Table B

Second Generation Antipsychotics (Atypical)

Risperidone

Study & Funding source	Studies that met criteria	Safety	Efficacy	Conclusions Limitations Comments
McDougle CJ, Scahill L, Aman MG, McCracken JT, Tierney E, Davies M, Arnold LE, Posey DJ, Martin A, Ghuman JK, Shah B, Chuang SZ, Swiezy NB, Gonzalez NM, Hollway J, Koenig K, McGough JJ, Ritz L, Vitiello B. Risperidone for the core symptom domains of autism: results from the study by the autism network of the research units on pediatric psychopharmacology. Am J Psychiatry. 2005 Jun;162(6):1142-8. PMID: 15930063 Funding Source: NIMH; NIH; Janssen Pharmaceutica supplied study medications.	RCT + POL Post hoc 8 wks + 16 wks 101 pts 5-17 yrs Autism	Not assessed in this study.	RCT Ritvo-Freeman Real Life Rating Scale Subscale / Change / ES Sensory/motor behaviors: RIS -0.41, PBO -0.02, 0.45 Social relationship: RIS -0.45, PBO -0.26, 0.68 Affective reactions: RIS -0.80, PBO -0.20, 1.10 Sensory responses: RIS -0.53, PBO -0.14, 0.77 Language: RIS -0.25, PBO -0.12, 0.81 Overall: RIS -0.49, PBO -0.15, 1.08 Children's Yale-Brown obsessive Compulsive Scale & Vineland Adaaptive Behavior Scales-maladaptive domain: Reduction in scores RIS > PBO. POL: No significant further change in above measures.	"Risperidone led to significant improvements in the restricted, repetitive, and stereotyped patterns of behavior, interests, and activities of austistic children but did not significantly change their deficit in social interaction and communication." p. 1142 "This pattern of treatment response was maintained for 6 months." p. 1142 Limitations: use of modified rating instruments that do not have established reliability and validity; short length, small sample size Comment: Gains obtained with RIS treatment by the end of 8 wks in the RCT were maintained over the next 16 wks of open-label treatment.
Shea S, Turgay A, Carroll A, Schulz M, Orlik H, Smith I, Dunbar F. Risperidone in the treatment of disruptive behavioral symptoms in children with autistic and other pervasive developmental disorders. Pediatrics. 2004 Nov;114(5):e634-41. Epub 2004 Oct 18. PMID: 15492353 Funding Source: Janssen-Ortho Inc., Canada; Johnson & Johnson Pharmaceutical Research and Development. Study used in FDA approval process.	RCT 8 wks 79 pts 5-12 yrs Pervasive Developmental Disorders	Most frequent Adverse Event on RIS: somnolence RIS: 72.5% PBO: 7.7% Most common AE on PBO: aggressive rx PBO: 20.5% Severe AE: RIS: 12.5% PBO: 5.1% Resolved without residual effects. Weight gain: RIS: +2.7 kg PBO: +1.0 kg Pulse rate, blood pressure (systolic): RIS > PBO EPS scores comparable between RIS & PBO Lab: No noteworthy difference between RIS & PBO.	Aberrant Behavior Checklist-Irritability change: RIS: -12.1 (64% improvement) PBO: -6.5 (31% improvement) P ≤0.001 Nisonger Child Behavior Rating Form Subscale / RIS / PBO / P Conduct: -10.4, -6-6, ≤0.001 Hyperactive: -8.1, -5.6, ≤ 0.05 Anxious: -4.6, -3.5, ≤ 0.05 Hypersensitive: -3.8, -2.7, ≤ 0.05 Clincial Global Impression-Change (Improvement) RIS: 87% PBO: 40%	"Risperdione was well tolerated and efficacious in treating behavioral symptoms associated with PDD in children." P. e634 "Most adverse events were self-limiting or readily manageable with dosing modifications." p. e640 Limitations: small sample size, short length, some other medications allowed Comment:

Table B

Second Generation Antipsychotics (Atypical)

Risperidone

Study & Funding source	Studies that met criteria	Safety	Efficacy	Conclusions Limitations Comments
Aman MG, Binder C, Turgay A. Risperidone effects in the presence/absence of psychostimulant medicine in children with ADHD, other disruptive behavior disorders, and subaverage IQ. J Child Adolesc Psychopharmacol. 2004 Summer;14(2):243-54. PMID: 15319021 Funding Source: Not documented in paper.	2 RCT's Post hoc 6 wks x 2 155 pts (pooled) 5-12 yrs Disruptive Behavior Disorders + subaverage IQ + ADHD	Most common Adverse Events Somnolence, headache, dyspepsia, rhinitis, vomiting Adverse Events No difference between RIS + STIM vs RIS + no STIM No difference in weight gain between RIS + STIM vs RIS + no STIM STIM = Stimulant medication	RIS Rating Scale % changes: RIS / No STIM / STIM N-CBRF Conduct: -44.2.3%* / -47.2%* Hyperact.: -36.5%* / -36.2%* ABC Irritability: -49.8%* / -43.9%* Hyperact.: -42.4%* / -40.6%* * p ≤ 0.0001 compared to placebo ° p = 0.0004 compared to placebo PBO Rating Scale % changes: PBO / No STIM / STIM N-CBRF Conduct: -24.3% / -10.9% Hyperact.: -21.2% / -11.4% ABC Irritability: -24.9% / -14.3% Hyperact.: -19.6% / -12.2%	"The addition of risperidone to a psychostimulant resulted in significantly better control of hyperactivity (p < 0.001) than was achieved with stimulant treatment alone, without causing an increase in adverse events.'" p. 243 "Risperidone was a safe and effective treatment, with or without a combined psychostimulant, for both disruptive behavior disorders and comorbid ADHD in children." p. 243 Limitations: post hoc analysis, no randomization of stimulant use, stimulant use held constant, multiple types of stimulants used Comment: Stimulants used: methylphenidate, dextroamphetamine, and pemoline. This is a complex post hoc analysis that pooled data from 2 different RCT's.
Findling RL, Kusumakar V, Daneman D, Moshang T, De Smedt G, Binder C. Prolactin levels during long-term risperidone treatment in children and adolescents. J Clin Psychiatry. 2003 Nov;64(11):1362-9. PMID: 14658952 Funding Source: Janssen-Ortho, Toronto, Ontario, Canada.	"RCT + POL" Post hoc pooled data from 5 trials: 2 RCT's + their 2 POL extensions + 1 standalone POL Up to 55 wks 700 pts 5-15 yrs Disruptive behavior disorders and subaverage intelligence	Prolactin levels in ng/ml (% at or above upper limit of normal): Pre-RIS: 7.8 (4.9%) RIS wks 4-7: 29.4 (70.5%) RIS wks 8-12: 23.4 RIS wks 16-24: 19.6 RIS wks 38-36: 18.5 RIS wks 40-48: 16.1 (30.7%) (RIS wks 52-55: 13.0) Female levels rose higher than males' but returned toward baseline more quickly. "Prepubertal females had mean levels within the normal range throughout the study." p. 1366 Side Effects Hypothetically Attributed to Prolactin (SHAP): There was no statistical difference in the percentage of patients who reported SHAP whether or not prolactin levels were normal or above the upper limit of normal. Prolactin levels did not vary with RIS dose.	Not assessed in this study.	"With long-term risperidone treatment in children and adolescents, serum prolactin levels tended to rise and peak within the first 1 to 2 months and then steadily decline to values within or very close to the normal range by 3 to 5 months." p. 1362 Limitations: post hoc, pooled data, no long term control group Comment: Side effects that could hypothetically be attributed to prolactin occur in populations not exposed to RIS or any other antipsychotic medication. It is difficult to interpret the data on SHAP without knowing the occurance rate of these symptoms in a control population. In any case the rate of these events in the experimental population is low and only 4 SHAP had not resolved by end of the study (3 gynecomastia and 1 menstual disorder).

Table B

Second Generation Antipsychotics (Atypical)

Risperidone

Study & Funding source	Studies that met criteria	Safety	Efficacy	Conclusions Limitations Comments
Snyder R, Turgay A, Aman M, Binder C, Fisman S, Carroll A; Risperidone Conduct Study Group. Effects of risperidone on conduct and disruptive behavior disorders in children with subaverage IQs. J Am Acad Child Adolesc Psychiatry. 2002 Sep;41(9):1026-36. PMID: 12218423 Funding Source: Not stated. One author is employee of Janssen-Ortho Inc., Toronto.	RCT 6 wks 110 pts 5-12 yrs Disruptive behaviors with subaverage IQ's	Adverse Events RIS: 86% PBO: 73.7 % Most common AE's: somnolence, headache, appetite increase, dyspepsia EPS: RIS: 13.2% PBO: 5.3% (Not significant difference.) Tardive dyskinesia: 1 pt in PBO group No pt discontinued due to AE's. ECG: no clinically significant changes Prolactin: RIS: no clinical symptoms PBO: 1 pt with dysmenorrhea Cognitive changes: No significant changes on testing in RIS condition Wt. gain: RIS: +2.2 kg PBO: +0.2 kg P < 0.001 (No effect of stimulant use on data.)	Change on Rating subscales pertinent to disruptive behaviors: Rating Scale / RIS / PBO / p N-CBRF Conduct: -15.8 / -6.8 / <.001 ABC Irritability: -20.8 / -4.2 / < .01 Hyperact.: -15.9 / -8.1 / < .01 BPI Aggression: -6.7 / -3.7 / < .01 RIS effect unaffected by diagnosis, ADHD, IQ, somnolence, or use of psychostimulants NCBRF = Nisonger Child Behavior Rating Form ABC = Aberrant Behavior Checklist BPI = Behavior Problems Inventory	"Risperidone appears to be an adequately tolerated and effective treatment in children with subaverage IQs and sever disruptive behaviors such as aggression and destructive behavior." (no page numbers on copy) Limitations: short length, lack of structured diagnostics, concomitant use of psychostimulants
Aman MG, De Smedt G, Derivan A, Lyons B, Findling RL; Risperidone Disruptive Behavior Study Group. Double-blind, placebo-controlled study of risperidone for the treatment of disruptive behaviors in children with subaverage intelligence. Am J Psychiatry. 2002 Aug;159(8):1337-46. PMID: 12153826 Funding Source: Janssen Research Foundation.	RCT 6 wks 118 pts 5-12 yrs Disruptive behaviors with subaverage IQs	Adverse Events: AE / PBO / RIS Total: 70% / 98% Somnolence: 10% / 51% Headache: 14% / 29% Vomiting: 6% / 20% Dyspepsia: 6% / 15% Weight gain: 2% / 15% Inc. prolactin: 2% / 13% Inc. appetite: 6% / 11% Rhinitis: 5% / 11% Most AE's were mild to moderate; no serious AE's reported. EPS: No differences between RIS and PBO. Lab: No differences between RIS and PBO. except prolactin. Prolactin: RIS > PBO for males; no associated with any clinical symptoms Weight gain: RIS: 2.2 kg PBO: 0.9 kg p 2 0.001 ECG: no clinically significant changes Cognitive tests: no RIS-related changes	Nisonger Child Behavior Rating Form conduct subscale change: Subscale / PBO / RIS Probl. Conduct: -6.2 / -15.2* Anxious: -3.0 / -8.4* Hyperactivity: -2.7 / -6.3* SIB/Stereotypy: -1.0 / -2.1** Ritualistic: -1.5 / -3.2** Hypersensitivity: -1.2 / -3.5* Compliant: 0.7 / 2.7* Adaptive: 0.1 / 1.6* * p < 0.001, ** p < 0.02	"Risperidone was effective and well tolerated for the treatment of severely disruptive behaviors in children with subaverage IQ." p. 1337 Limitations: short length, concomitant use of psychostimulants and select other meds

Table B

Second Generation Antipsychotics (Atypical)

Risperidone

Study & Funding source	Studies that met criteria	Safety	Efficacy	Conclusions Limitations Comments
McCracken JT, McGough J, Shah B, Cronin P, Hong D, Aman MG, Arnold LE, Lindsay R, Nash P, Hollway J, McDougle CJ, Posey D, Swiezy N, Kohn A, Scahill L, Martin A, Koenig K, Volkmar F, Carroll D, Lancor A, Tierney E, Ghuman J, Gonzalez NM, Grados M, Vitiello B, Ritz L, Davies M, Robinson J, McMahon D; Research Units on Pediatric Psychopharmacology Autism Network. Risperidone in children with autism and serious behavioral problems. N Engl J Med. 2002 Aug 1;347(5):314-21. PMID: 12151468 Funding Source: NIMH; NIH; Korczak Foundation. Janssen Pharmaceutica supplied study medications. Study used in FDA approval process.	RCT 8 wks 101 pts 5-17 yrs Autism with severe tantrums, aggression or SIB	Adverse Events more common in RIS vs PBO: Increased appetite Fatigue Drowsiness Drooling No serious AE's reported. Wt. gain: RIS: 2.7 kg PBO: 0.8 kg P < 0.001 EPS: none in either group by rating scale. Rate of withdrawal from study: RIS: 6% PBO: 35% No withdrawals due to Adverse Effects in RIS group. Many withdrawals in PBO group due to lack of efficacy.	Aberrant Behavior Checklist-Irritability % score change: RIS: -56.9% PBO: -14.1% P < 0.001 Positive response (≥25% reduction ABC-Irritability and CGI-I of much/very much improved) RIS: 69% PBO: 12% P < 0.001 CGI-I = Clinical Global Impression –Improvement subscale	"Risperidone was effective and well tolerated for the treatment of tantrums, aggression, or self-injurious behavior in children with autistic disorder." p. 314 Limits: short length Comment: Rates of withdrawal tend to be higher in placebo groups because the parents perceive their children are not sufficiently improving and motivation to continue is low. Paper notes that studies of HAL in same population produce 15-20% difference between HAL and PBO while this study of RIS produced a difference of 43%. The HAL paper referenced is from 1989. p. 320
Gaffney GR, Perry PJ, Lund BC, Bever-Stille KA, Arndt S, Kuperman S. Risperidone versus clonidine in the treatment of children and adolescents with Tourette's syndrome. J Am Acad Child Adolesc Psychiatry. 2002 Mar;41(3):330-6. PMID: 11886028 Funding Source: Not documented in paper.	RCT 8 wks 21 pts 7-17 yrs Tourette's	Adverse Events Adverse Event / RIS / CLD Total / 33% / 58% sedation / 11% / 42% dizziness / 11% / 17% stiffness / 22% / 8% dry mouth / – / 8% wt gain / 2.1 kg / 0.1 kg inc. prolactin / 2% / 13% EPS / □ / □ Lab / □ / □ ECG / □ / □ , not reported □groups statistically equivalent □No significant changes CLD = Clonidine	Yale Global Tic Severity Scale change: RIS: -21% CLD: -26% % Obsessive Compulsive symptoms response rate: RIS: 63% CLD: 33% Difference not significant. Scale / RIS / CLD / p YGTSS / -10.9 / -13.8 / 0.728 Y-BOCS / -6.3 / -2.8 / 0.880 AHDHRS / -9.9 / -11.2 / 0.988 p values reflect that there is no significant difference between outcomes with RIS vs CLD. CLD = Clonidine	"In this pilot study, risperidone demonstrated efficacy equivalent to clonidine in the treatment of tic symptoms in children and adolescents with TS." (no page number in copy) Limitations: short length, small sample size, no placebo control, few female pts Comment: "Many researchers and institutional review boards consider the use of placebo groups in clinical trials of major neuropsychiatric illnesses to be unethical when known effective treatments are available." (no page numbers in copy) Choice of CLD as comparator was appropriate in place of placebo. Study underpowered to show differential response of OC symptoms, but possible greater effectiveness of RIS is hinted.

Table B

Second Generation Antipsychotics (Atypical)

Risperidone

Study & Funding source	Studies that met criteria	Safety	Efficacy	Conclusions Limitations Comments
Buitelaar JK, van der Gaag RJ, Cohen-Kettenis P, Melman CT. A randomized controlled trial of risperidone in the treatment of aggression in hospitalized adolescents with subaverage cognitive abilities. J Clin Psychiatry. 2001 Apr;62(4):239-48. PMID: 11379837 Funding Source: Janssen-Cilag BV. Tilburge, the Netherlands.	RCT 6 wks 38 pts Mean age = 14.0 Aggression in disruptive behavior disorders + subaverage IQ	Adverse Events AE / RIS / PBO / p Total / 89% / 58% / 0.06 Tiredness / 11 / 1 Sleep probl. / 2 / 5 Headache / 4 / 0 Sialorrhea / 4 / 0 Nausea / 3 / 0 Wt gain / 2.3 kg / 0.6 kg Inc. prolactin / +16.8 / -5.4 / <.01 EPS / +0.6 / -0.5 / <.05 Lab / □ / □ ECG / □ / □ □No significant changes 1 pt temporarily withdrew due to nausea. No prolactin related AEs reported. EPS rating scale showed significant increase in Parkinsonism for RIS.	Rating Scale/Subscale Changes Scale / RIS / PBO / p CGI-S Total / -1.6 / +0.2 / <.001 M. disturbed / -58% / +5% / NR OAS-M Ward / -4.8 / -0.9 / NS School / -1.9 / -r.5 / NS ABC Ward / -17.6 / -5.2 / < .05 School / -14.9 / -3.7 / < .05 NR = Not reported NS = Not significant CGI-S = Clinical Global Impression-Severity OAS-M = modified Overt Aggresion Scale ABC = Aberrant Behavior Checklist	"These results suggest that risperidone may be effective for severe aggression in adolescents with disruptive behavior disorders and subaverage intelligence, and these results are consistent with reports suggesting its effectiveness for treating severe aggression in adolescents in general." p. 239 Limitations: short length, small sample size, predominance of males in sample, heterogeneity of diagnoses, preponderance of males in sample Comment: Subjects were institutionalized due to chronic refractory repetitive aggression. Not enough pts to analyze by IQ level.
Van Bellinghen M, De Troch C. Risperidone in the treatment of behavioral disturbances in children and adolescents with borderline intellectual functioning: a double-blind, placebo-controlled pilot trial. J Child Adolesc Psychopharmacol. 2001 Spring;11(1):5-13. PMID: 11322745 Funding Source: Janssen Pharmaceutica, Berchem, Belgium.	RCT 4 wks 13 pts 6-14 yrs Behavioral disturbances + borderline intelligence	Adverse Events AE / RIS / PBO / p Total / 4 / 2 Somnolence / 1 / 0 BP, HR / □ / □ Weight gain / 1.8 kg / 0.6 kg / .319 Inc. prolactin / NM / NM EPS scale / □ / □ / .601 Lab / NM / NM ECG / NM / NM All pts completed study.	Rating Scale/Subscale Changes Scale / RIS / PBO / p ABC Total % imp. / - 65% / -7% Total score / -30.3 / -3.3 / < .01 Irritation / -10.8 / 0.1 / < .01 Hyperactivity / -14.8 / 10. / < .01 CGI Mean score / -2.2 / -0.2 / < .05 # 5t VMI / 5 / 0 / NA VAS ind. target / -40.5 / 1.7 / <.001 PAC Social rel. / 1.3 / 0.1 / < .05 Oc. attitudes / 0.7 / -0.6 / < .05 PAC score positive change denotes improvement.	"In conclusion, short-term risperidone treatment was well tolerated and significantly more effective than placebo in controlling behavioral disturbance in children with low IQ." p. 5 Limitations: small sample size, Comment: Unusually, study had more females than males. (8 girls, 5 boys)
Haas M, Karcher K, Pandina GJ. Treating disruptive behavior disorders with risperidone: a 1-year, open-label safety study in children and adolescents. J Child Adolesc Psychopharmacol. 2008 Aug;18(4):337-45. PMID: 18759643 Funding Source: Johnson & Johnson Phramaceutical Research & Development	POL 1 yr 232 pts 5-17 yrs Disruptive behavior disorders	65% overall experienced Adverse Events (mostly mild to moderate) 3.4% discontinued due to AE's. Weight gain: 4.3 kg over all pts. EPS: 4.3% Prolactin up with RIS but decreased over time. Cardiac changes not clinically significant. Majority of AE's were related to psychiatric disorder.	Nisonger Child Behavior Rating Form-Conduct Problem Subscale: RIS/RIS: -3.7 PBO/RIS: -5.9 Those previously on placebo improved the most.	"Risperidone reinitiated for DBD in children with normal intelligence quotients (IQ) was safe and well tolerated over an additional year of treatment." Limitations: inclusion only of patients who had previous treatment response (self-selection bias), open label, use of other meds during study Comment: Participants were patients who had just completed a blinded placebo controlled study of risperidone.

Table B

Second Generation Antipsychotics (Atypical)

Risperidone

Study & Funding source	Studies that met criteria	Safety	Efficacy	Conclusions Limitations Comments
Capone GT, Goyal P, Grados M, Smith B, Kammann H. Risperidone use in children with Down syndrome, severe intellectual disability, and comorbid autistic spectrum disorders: a naturalistic study. J Dev Behav Pediatr. 2008 Apr;29(2):106-16. PMID: 18349709 Funding Source: Not documented in paper.	POL Mean study length = 95.8 days 23 pts 3-12 yrs Down syndrome with severe intellectual disability and autism spectrum disorder	Adverse Events Hyperphagia 48% Wt. gain: +2.8 kg Sedation & EPS in one participant that responded to dosage decrease.	Aberrant Behavior Checklist changes Subscale / Change / ES Irritability -5.1 0.54 Lethargy -6.2 0.71 Stereotypy -3.2 0.68 Hyperactivity -7.7 0.77 Inapp.speech -1.0 0.35 Sleep: 70% had sleep disturbance at beginning of study. At end 9% had sleep disturbance.	"These findings support our clinical impression of improvement on important target behaviors such as aggression, disruptiveness, self-injury, stereotypy, and social withdrawal. Low-dose risperidone appears to be well tolerated in children with DS+ASD, although concerns about weight gain and metabolic alterations may limit its usefulness over the long term in some children." Limitations: open label, no randomization, lack of control group, behavioral outcomes rated by parents, diagnostic heterogeneity, no control for other treatments, behavioral comorbidity Comment: Sleep also improved which is a family quality of life issue as well as youth issue.
Erdogan A, Atasoy N, Akkurt H, Ozturk D, Karaahmet E, Yalug I, Yalug K, Ankarali H, Balcioglu I. Risperidone and liver function tests in children and adolescents: a short-term prospective study. Prog Neuropsychopharmacol Biol Psychiatry. 2008 Apr 1;32(3):849-57. Epub 2008 Jan 12. PMID: 18258348 Funding Source: Not documented in paper.	POL 1 mo 120 pts 3-17 yrs Treatment with risperidone (All psychiatric diagnoses included)	Liver Function Test Changes Test / Change / p ALT +3.88 0.0001 AST +12.31 0.0001 GGT +6.16 0.0001 ALP +122.30 0.0001 DB +0.02 0.011 IDB +0.05 0.013 Overall 52.5% showed asymptomatic increases in liver enzymes and bilirubin. Only one participant showed a marked elevation (0.8%).	Efficacy was not assessed in this study.	"These findings suggest that risperidone in short-term treatment may lead to evidence of asymptomatic liver function test abnormalities, however it rarely may cause marked liver function test abnormalities at therapeutic doses in children and adolescents." p. 856 Limitations: open label, short length, use of other meds during study, variation in age of participants Comments: Data is similar to that seen in adult studies.
Holzhausen SP, Guerreiro MM, Baccin CE, Montenegro MA. Use of risperidone in children with epilepsy. Epilepsy Behav. 2007 May;10(3):412-6. Epub 2007 Mar 26. PMID: 17382594 Funding Source: FAPESP Grant.	POL 3 mos 54 pts 2-18 Epilepsy and self-injurious, aggressive, or destructive behavior	Seizure exacerbation: 4% Risperidone withdrawn in 16 patients (18.5%) for lack of efficacy and in 5 (9.2%) for adverse events: Seizure exacerbation: 2 pts Agitation: 2 pts Somnolence: 1 pt	Improvement in behavior: 70.4%	"Our data suggest that risperidone can be used in pediatric patients with epilepsy and that seizure outcome is not changed in most children with epilepsy and psychiatric comorbidity. In addition, behavior improvement is usually achieved in most patients." p. 412 Limitations: open label, no control group, heterogeneous epilepsy diagnosis, multiple epilepsy medications used simultaneously, no use of rating scales

Table B

Second Generation Antipsychotics (Atypical)

Risperidone

Study & Funding source	Studies that met criteria	Safety	Efficacy	Conclusions Limitations Comments
Troost PW, Althaus M, Lahuis BE, Buitelaar JK, Minderaa RB, Hoekstra PJ. Neuropsychological effects of risperidone in children with pervasive developmental disorders: a blinded discontinuation study. J Child Adolesc Psychopharmacol. 2006 Oct;16(5):561-73. PMID: 17069545 Funding Source: Korczak Foundation; Study medications donated by Janssen Cilag BV.	POL + RCT (RCT Discontiuation study) 24 wks + 8 wks 24 pts 5-17 yrs Pervasive Developmental Disorders	Not assessed in this study.	Focused attention: No RIS effect noted Divided attention (Serial search in working memory) Open label compared with RCT discontinuation: RIS: improved PBO: regressed	"In conclusion, the present study suggests a possible additional benefit of risperidone in low-to-intermediate doses in enhancing working memory performance in children with PDDs. This may be associated with improvements in social, communicative, and academic functioning." p. 571 Limitations: large proportion (~50%) of participants unable to produce valid task results leading to even smaller sample size, Comments: Cognitive testing in individuals with PDD's is difficult and more so in younger subjects. Working memory is known to be deficient in PDD's: however, focused attention may not be deficient in PDD and so treatment effects would not be expected.
Pavuluri MN, Henry DB, Carbray JA, Sampson GA, Naylor MW, Janicak PG. A one-year open-label trial of risperidone augmentation in lithium nonresponder youth with preschool-onset bipolar disorder. J Child Adolesc Psychopharmacol. 2006 Jun;16(3):336-50. PMID: 16768641 Funding Source: Marshall Reynolds Foundation, NIH, Campus Research Board Award, Janssen Research Foundation.	POL 1 yr 38 pts 4-17 yrs Bipolar Disorder (Preschool onset Lithium nonresponders)	2 pts withdrew due to lithium intolerance AE's: no significant difference between groups Weight gain: +3.5 kg (within CDC expected limits) Asymptomatic prolactin elevation 2 pts Other lab were normal.	Response on Young Mania Rating Scale (≥50% decrease from baseline): Lithium alone: 17/38 21 non-responders Of the 21 lithium non-responders, with RIS added: 18/21 or 85.7%	"A substantial proportion of youth with a history of preschool-onset BD treated with lithium were either nonresponders or partial responders. Subsequent augmentation of lithium with risperdione in these cases was well tolerated and efficacious." p. 336 "Significant predictors of inadequate response to lithium monotherapy requiring augmentation were: (1) attention-deficit/hyperactivity disorder (ADHD), (2) severity at baseline, (3) history of sexual or physical abuse, and (4) preschool age." p. 336 Limitations: diagnosis of preschool onset was retrospective, lack of diagnostic instruments for preschoolers, small sample size, no randomization of nonresponders, other med use permitted

Table B

Second Generation Antipsychotics (Atypical)

Risperidone

Study & Funding source	Studies that met criteria	Safety	Efficacy	Conclusions Limitations Comments
Reyes M, Croonenberghs J, Augustyns I, Eerdekens M. Long-term use of risperidone in children with disruptive behavior disorders and subaverage intelligence: efficacy, safety, and tolerability. J Child Adolesc Psychopharmacol. 2006 Jun;16(3):260-72. PMID: 16768634 Funding Source: Johnson & Johnson Pharmaceutical Research and Development.	POL 1 yr (Second yr extension after previous 1 yr study) 48 pts 6-15 yrs Disruptive Behavior Disorders (subaverage intelligence)	Adverse Events decreased compared to original 1 yr of treatment. 13% (6 pts) discontinued due to AE's: Worsening conduct disorder, hyperkinesias, Gyneocmastia (2 pts), pain, and depression Prolactin: generally increased, with 1 pt as significant high outlier. The 2 pts with severe gynecomastia had normal prolactin levels. No effect on sexual maturation. Extrapyramidal Symptoms: 2 children 3 adolescents all mild to moderate No tardive dyskinesia No clinically significant lab changes: Hematology, chemistry, glucose, or urinalysis Weight gain observed in original 1 yr stabilized during this second yr.	Nisonger Child Behavior Rating Form—conduct subscale: Beginning of orinigal study: 32.3 At end Yr 1: 15.2 At end Yr 2: 16.5 $p < 0.001$ Improvement maintained. Aberrant Behavior Checklist: Gains achieved in first year maintained in second year. Clinical Global Impression: Gains achieved in first year maintained in second year. Cognitive testing showed small improvement, but no statistical tests performed on data.	"Risperidone is safe and effective in treating DBDs in children over a cumulative period of 2 years" p. 260 Limitations: no control, small sample size, open label
Williams SK, Scahill L, Vitiello B, Aman MG, Arnold LE, McDougle CJ, McCracken JT, Tierney E, Ritz L, Posey DJ, Swiezy NB, Hollway J, Cronin P, Ghuman J, Wheeler C, Cicchetti D, Sparrow S. Risperidone and adaptive behavior in children with autism. for vertical spacing only J Am Acad Child Adolesc Psychiatry. 2006 Apr;45(4):431-9. PMID: 16601648 Funding Source: NIMH (RUPP).	POL 6 mos 48 pts 5-16 yrs Autism	Not assessed in this study.	Vineland Scales Age-equivalents (mos) in domains: Comm = Communication DL = Daily living skills Soc = Socialization Comp = Composite Domain / Change / ES Comm 4.79 0.20 DL 4.42 0.27 Soc 7.79 0.45 Comp 5.67 0.33	"Although limited by the absence of a control group, these results suggest that risperidone may improve adaptive skills in children with autistic disorder accompanied by serious behavioral problems." p. 431 Limitations: small sample size, no control group, sample selected for severe behavioral problems, short length Comment: Computed effect sizes (ES) show the measured changes to be not meaningful to only small/moderate by the data in this study. Change in measured socialization is of moderate effect size though and this is a core deficiency area in autism.

Table B

Second Generation Antipsychotics (Atypical)

Risperidone

Study & Funding source	Studies that met criteria	Safety	Efficacy	Conclusions Limitations Comments
Reyes M, Olah R, Csaba K, Augustyns I, Eerdekens M. Long-term safety and efficacy of risperidone in children with disruptive behaviour disorders. Results of a 2-year extension study. Eur Child Adolesc Psychiatry. 2006 Mar;15(2):97-104. PMID: 16523250 Funding Source: Not documented in paper. Three authors are employees of Johnson & Johnson or a related company.	POL 2 yrs (Extension of previous 1 yr study) 35 pts 6-16 yrs Disruptive Behavior Disorders	Few extrapyramidal symptoms occurred and no tardive dyskinesia Most pts. scored 0 at all measurements. ECG's, vital signs, lab: no clinically significant changes. ECG's Adverse Events: most mild and none could be definitively related to risperidone BMI: Modest increase part of which is normal growth; measurements stable from end of first through end of third years. Normal growth and sexual maturation	Clinical Global Impression-Severity Scores Baseline: Score 5.6, Meaning Severe Year 1: Score 2.9, Meaning Mild Year 3: Score 3.1, Meaning Mild	"Continuing low-dose risperdione for up to 3 years appears to be safe and effective in children with disruptive behaviour disorders." p. 97 Limitations: small sample size, open label Comment: Most weight gain occurred in first 6 months of treatment prior to beginning of this study.
Research Units on Pediatric Psychopharmacology Autism Network. Risperidone treatment of autistic disorder: longer-term benefits and blinded discontinuation after 6 months. Am J Psychiatry. 2005 Jul;162(7):1361-9. PMID: 15994720 Funding Source: NIMH; NIH; Korczak Foundation; Janssen Pharmaceutica supplied study medications. Study used in FDA approval process.	POL + RCT 4 mos + 8 wks 63 + 38 pts 5-17 yrs Autism with severe tantrums, aggression, and/or self-injurious behavior and previous + response to RIS	POL maintenance study: Discontinuation due to Adverse Events: 1 pt Weight gain: 5.1 kg p <0.0001 Common AE's: Increased appetite Tiredness Drowsiness No extrapyramidal symptoms.	POL maintenance study: Aberrant Behavior Checklist-Irritability change from beginning of maintenance: +1.2 Change was small and clinically insignificant From initiation of RIS treatment -15.8 ES >1.0 (!) Change is large and stable. Clinical Global Impression-Improvement 82.5% rated as much/very much improved RCT discontinuation study: Relapse Rates: RIS: 12% PBO: 62.5% Mean survival time to relapse: RIS: 57 days PBO: 34 days	"Risperidone showed persistent efficacy and good tolerability for intermediate-length treatment of children with autism characterized by tantrums, aggression, and/or self-injurious behavior. Discontinuation after 6 months was associated with a rapid return of disruptive and aggressive behaviour in most subjects." p. 1361 Limitations: short length compared to actual clinical practice, flexible dosing Comment: Discontinuation phase was stopped by the NIMH Data and Safety Monitoring Board because of the high rate of relapse of the participants in the placebo arm. These patients were then treated clinically.
Biederman J, Mick E, Wozniak J, Aleardi M, Spencer T, Faraone SV. An open-label trial of risperidone in children and adolescents with bipolar disorder. J Child Adolesc Psychopharmacol. 2005 Apr;15(2):311-7. PMID: 15910215 Funding Source: Janssen Pharmaceutica.	POL 8 wks 30 pts 6-17 yrs Bipolar Disorder	Adverse Events Weight gain: 2.1 kg < 0.001 Prolactin: 4x increase, p < 0.001	Responded (Clinical Global Impression-Improvement in Mania ≤2) = 70% Young Mania Rating Scale change: -14.4 p < 0.0001	"Open-label risperidone treatment was associated with a significant short-term improvement of symptoms of pediatric bipolar disorder." p. 311 Limitations: small sample size, short length. open label

Table B

Second Generation Antipsychotics (Atypical)

Risperidone

Study & Funding source	Studies that met criteria	Safety	Efficacy	Conclusions Limitations Comments
Croonenberghs J, Fegert JM, Findling RL, De Smedt G, Van Dongen S; Risperidone Disruptive Behavior Study Group. Risperidone in children with disruptive behavior disorders and subaverage intelligence: a 1-year, open-label study of 504 patients. J Am Acad Child Adolesc Psychiatry. 2005 Jan;44(1):64-72. PMID: 15608545 Funding Source: Johnson & Johnson Pharmaceutical Research and Development.	POL 1 yr 504 pts 5-14 yrs Disruptive Behavior Disorders (with subaverage intelligence)	91% of patients experienced an Adverse Event. Most common AE's: Somnolence 30% Rhinitis 27% Headache 22% Weight gain 17% AE's causing study withdrawal by 3 or more pts: Weight gain: 9 pts Increased appetite: 4 pts Gynecomastia: 3 pts Somnolence: 3 pts Headache: 3 pts Weight gain: +1.9 kg (Most occurred in first 6 months of RIS) Extrapyramidal Symptoms: mean ESRS scores decreased during RIS treatment. –0.4 $p < 0.001$ Dyskinesia: 2 pts (resolved with medication withdrawal, unclear if tardive dyskinesia) Lab: no clinically significant changes Prolactin: peaked at wk 4 and then decreased back into normal range. Except for 1 pt, all AE's possibly related to increased prolactin were mild and resolved spontaneously. Sexual maturation proceeded normally. ECG, vital signs: No clinically significant changes	Nisonger Child Behavior Rating Form subscales change: Conduct Problem: -15.8 Compliant/calm: +3.4 Adaptive/social: +1.9 Insecure/anxious: -5.4 Hyperactive: -6.8 Self-injury/stereotypic: -1.0 isolated/ritualistic: -1.7 overly sensitive: -2.1 All: $p < 0.001$ Clinical Global Impression-Severity: 66% rated as not ill or having only mild symptoms at endpoint. (72% rated marked to extremely severe symptoms at baseline) Aberrant Behavior Checklist: -28.3 $p < 0.001$	"Risperdione was well tolerated and effective in the long-term treatment of disruptive behavior disorders in children with subaverage intelligence." (no page numbers in copy obtained) Limitations: open label, no control group, limited population studied (subaverage intelligence), severe symptoms, other med used allowed
Martin A, Scahill L, Anderson GM, Aman M, Arnold LE, McCracken J, McDougle CJ, Tierney E, Chuang S, Vitiello B. Weight and leptin changes among risperidone-treated youths with autism: 6-month prospective data. Am J Psychiatry. 2004 Jun;161(6):1125-7. PMID: 15169706 Funding Source: NIMH; NIH; Korczak Foundation. (RUPP)	POL 6 mos 63 pts 5-17 yrs Autism	Adverse Events Weight gain: +5.6 kg BMI gain: +20. kg/m^2	Not assessed in this study.	"Chronic risperidone exposure in children with autism causes weight gain in excess of developmentally expected norms that follows a curvilinear trajectory and decelerates over time. Serum leptin change does not reliably predict risperidone-associated weight gain." p. 1125 Limitations: small sample size, short length, open label, no control group Comment: "Notably weight gain at 1 month emerged as a powerful predictor of later weight gain in this study." p. 1126

Table B

Second Generation Antipsychotics (Atypical)

Risperidone

Study & Funding source	Studies that met criteria	Safety	Efficacy	Conclusions Limitations Comments
Gagliano A, Germanò E, Pustorino G, Impallomeni C, D'Arrigo C, Calamoneri F, Spina E. Risperidone treatment of children with autistic disorder: effectiveness, tolerability, and pharmacokinetic implications. J Child Adolesc Psychopharmacol. 2004 Spring;14(1):39-47. PMID: 15142390 Funding Source: Not documented in paper.	POL 24 wks 20 pts 3-10 yrs Autism	Adverse Events Prolactin: increased in all children, but then decreased in some pts; no clinical symptoms noted Weight gain: 3.7 kg Extrapyramidal Symptoms: none	Responders (≥25% decrease on CPRS-14 and CGI Improvement of much/very much improved): 8 pts (40%) Further 10 pt slightly improved (50%) 2 pts no improvement (10%) CPRS-14 Mean change: -10.8 $p < 0.01$ CPRS-14 = 14 selected items from Children's Psychiatric Rating Scale	"This study provides additional evidence of the beneficial effects of risperidone in children with autistic disorder. However, the potential advantages of risperidone should be weighed agaist the risk of unwanted effects." p. 45 Limitations: open label, lack of placebo control, small sample size, lack of use of standardized diagnostic instrument, short length, lack of in depth analysis by age Comment: Improvement obtained was evident by 12 wks with no further improved by 24 wks. Lower response was obtained with the youngest patients (3-4 years). Core negative symptoms (social withrawal and uncooperative behavior) respond little if at all. No doses higher than 2 mg used in study.
Findling RL, Aman MG, Eerdekens M, Derivan A, Lyons B; Risperidone Disruptive Behavior Study Group. Long-term, open-label study of risperidone in children with severe disruptive behaviors and below-average IQ. Am J Psychiatry. 2004 Apr;161(4):677-84. PMID: 15056514 Funding Source: Johnson & Johnson Pharmaceutical Research and Development.	POL 48 wk 107 5-12 Severe Disruptive Behaviors + below-average IQ	Most common Adverse Events: Somnolence: 33% Headache: 33% Rhinitis: 28% Weight gain: 21% Weight gain: 5.5 kg (half was developmentally expected growth) Prolactin: transient, asymptomatic increases (peak at wk 4) EPS: no changes in rating scales; no tardive Dyskinesia ECG: no clinically significant changes	Nisonger Child Behavior Rating Form: By week 4, scores for those who had previously been on PBO in the preceding RCT were similar to those who had received RIS all along. Overall change: 6 + 48 wks RIS: -14.6 48 wks RIS: -14.3	"Long-term risperidone appears to be generally safe, well tolerated, and effective for treating severely disruptive behaviors in children with subaverage intelligence." Limitations: more male pts than female, use of body weight rather than BMI for analysis, open label, no control group
Turgay A, Binder C, Snyder R, Fisman S. Long-term safety and efficacy of risperidone for the treatment of disruptive behavior disorders in children with subaverage IQs. Pediatrics. 2002 Sep;110(3):e34. PMID: 12205284 Funding Source: Janssen-Ortho Inc.	POL (Extension of previous RCT) 48 wks 77 pts 5-12 yrs Disruptive behavior disorders and subaverage IQs	Most common Adverse Events: Somnolence, headache, weight gain None severe No evidence of cognitive deterioration on Continuous Performance Test, MVLT-C: cognitive function improved on both tests. Prolactin: peaked at 4 wks and declined Wt. gain: +7.1 kg, $P < .001$ Change significant at endpoint only for males. No clinical manifestations in either sex. 2 pts discontinued due to AE's: headache 1 headache and dyspnea 1 both occurred after > 200d tx EPS: ~25% of pts, none severe TD: none	Nisonger Child Behavior Rating Form Subscale score changes from previous RCT baseline to endpoint of POL extension: Subscale / RIS / RIS*** Prob. Conduct: -16.9 / -18.1 Anxious: -7.76 / -6.42 Hyperactactivity: -7.97 / -8.18 SIB/Stereotypy: -1.65 / -1.31 Ritualistic: -3.05 / -2.38 Hypersensitivity: -2.42 / -3.36 Compliant: 2.97 / 3.54 Adaptive: 1.46 / 2.21 ***RIS = pt who received PBO in the RCT but then were placed on RIS for this POL extension. $p < 0.05$ or better for all data	"Risperidone, administered as an oral solution at a mean dose of 1.38 mg/d (range: 0.02-0.06 mg/kg/d) for 1 year, was well tolerated, safe, and showed maintenance of effect in the treatment of disruptive behavior disorders in children aged 5 to 12 years with subaverage IQ's." p. 2 Limitations: open label, small sample size, concomitant use of psychostimulants Comments: Rates of TD with HAL and other FGA's are high in pts with IDDs, in neighborhood of 7-12%. (p. 9) after <1.5 yrs. Analysis showed that sedation side effect did not play a role in treating disruptive behaviors. No TD in this study of RIS.

Table B

Second Generation Antipsychotics (Atypical)

Risperidone

Study & Funding source	Studies that met criteria	Safety	Efficacy	Conclusions Limitations Comments
Malone RP, Maislin G, Choudhury MS, Gifford C, Delaney MA. Risperidone treatment in children and adolescents with autism: short- and long-term safety and effectiveness. J Am Acad Child Adolesc Psychiatry. 2002 Feb;41(2):140-7. PMID: 11837403 Funding Source: NIMH in part.	POL 1 mo + 6 mos 22 pts 2.9-16.3 yrs Autism	Adverse Events AE / 1 m / 6 m Total sedation / 68.1 / 42% Constipation / 2 pts / 0 Headache / 1 pt / 0 Drooling / 1 pt / 0 Inc. activity / 1 pt / 0 Diurnal enuresis / 1 pt / 1 pt Nausea/vomiting / 0 / 1 Polyuria/polydip / 0 / 1 Pain in extremity / 0 / 1 Febrile seizures / 0 / 2 Inc. appetite / 31.8% / +++ Weight gain / 2.57 kg / 7.33 kg Inc. prolactin / NR / NR EPS / 0 / 0* Lab / 0 / 0 ECG / 0 / 0 *2 pts (15.4 %)developed reversible dyskinesias after RIS withdrawn	Rating Scale/Subscale Changes Scale / 1 m / 6 m / ES CPRS-14 Total / -0.82 / / -1.26 Autism / -0.65 / / -0.92 Anger / -1.35 / / -1.03 Hyperactivity / -0.87 / / -0.86 Speech dev. / -0.10 / / -0.12 CGI-S / -0.67 / / .003* CGI-I / 77.3% / 91% / NR * p value (not Effect Size) NR – not reported After discontinuation: All pts have worsening of symptoms: Very much worse: 13% Much worse: 54% Minimally worse: 23%	"Risperidone shows promise as a treatment in autism. However, withdrawal dyskinesias were noted." (no page numbers in copy) Limitations: no control group, open label, lack of parental ratings, only one outcome scale at 6 mos Comment: Effect size for RIS on the CPRS was very large at –1.26.
Masi G, Cosenza A, Mucci M, Brovedani P. Open trial of risperidone in 24 young children with pervasive developmental disorders. J Am Acad Child Adolesc Psychiatry. 2001 Oct;40(10):1206-14. PMID: 11589534 Funding Source: Not documented in paper.	POL 16 wks 24 pts 3.6-6.6 yrs Pervasive developmental disorders	Adverse Events AE / over 4 m Total / 45.9% Sedation / 1 pt Agitation / 1 pt Enuresis / 3 pts Dec. appetite / 3 pts Inc. appetite / 6 pts Weight gain / 1.13 kg Inc. prolactin / Not measured EPS / 1 pt Lab / 0 ECG / 0 Failure to complete due to AEs: 2 pts sedation & hyporexia Tachycardia without ECG changes or symptoms	Rating Scale/Subscale Changes Scale / 4 m / p CPRS-14 / -11.14 / < .001 CARS / -6.4 / < .001 CGI-I / 36.4%* / NR C-GAS / 8.27 / <.001 *Rated as much/very much improved CPRS-14 = Children's Psychiatric Rating Scale, 14 selected items CARS = Childhood Autism Rating Scale CGI-I = Clinical Global Impression-Improvement C-GAS = Children's Global Assessment Scale	"Low-dose risperidone may positively affect symptoms in yourg autistic children, improving disruptive/hyperactive behavior and affective dysregulation." (no page numbers in copy) Limitations: no placebo control, low dosage RIS, rating scales administered only 2 times, use of other rating scales may have been desireable
Submitted item: Does not meet paper type and date criteria. Waring EW, Dewan VK, Cohen D, Grewal R. Risperidone as an adjunct to valproic acid. Can J Psychiatry. 1999 Mar;44(2):189. Letter. PMID: 10097843 Funding Source: Not applicable.	Letter NA 1 pt 50 yrs Refractory Mania	Not assessed in this letter.	Man with 32 yr history of chronic relapsing mania achieved remission of psychosis and mania when risperidone was added as an adjunct medication to valproic acid.	"Other studies have suggested that risperidone as an adjunct totreatment offers advantages over conventional antipsychotics or mood stabilizers for treating psychosis, agitation, and cycling accompanying affective illness." p. 189. Limitations: anecdote, adult report

Table B

Second Generation Antipsychotics (Atypical)

Risperidone

Study & Funding source	Studies that met criteria	Safety	Efficacy	Conclusions Limitations Comments
Submitted item: Does not meet paper type and date criteria. Kumra S, Herion D, Jacobsen LK, Briguglia C, Grothe D. Case study: risperidone-induced hepatotoxicity in pediatric patients. J Am Acad Child Adolesc Psychiatry. 1997 May;36(5):701-5. PMID: 9136506 Funding Source: Not documented in paper.	Case Series 7 mos –17 mos 13 pts 6-18 yrs Pediatric patients treated with risperidone over a 2 yr 4 mo period	Two male children presented with obesity, liver enzyme abnormalities with confirmatory evidence of fatty liver. In each case liver damage reversed after withdrawal of risperidone and/or weight loss.	Not assessed in this case series.	"The observations suggest that long-term risperidone therapy is possibly associated with hepatotoxicity in male pediatric patients." p. 701. Limitations: retrospective, no control, small sample size Comment: ?Not borne out by later RCT's and POL's? "Many aspects of the cases presented in this report resemble the clinical descriptions of steatohepatitis in obese children and adolescents..." p. 703 "it has now been recognized that some obese patients (taking no medications) with non-alcoholic hepatitis have a severe, progressive liver disease that can lead to cirrhosis, although this finding is controversial." p. 703. Currently it is thought that high levels of fructose in the diet (as in high fructose corn syrup) trigger metabolism by the same pathway used for ethanol that produces fatty liver and cirrhosis. This also leads to the "soda" belly that is analogous to "beer" belly, where large amounts of adipose tissue accumulate at the waistline. [ref needed]
Submitted item: Does not meet date criteria. Findling RL, McNamara NK, Branicky LA, Schluchter MD, Lemon E, Blumer JL. A double-blind pilot study of risperidone in the treatment of conduct disorder. J Am Acad Child Adolesc Psychiatry. 2000 Apr;39(4):509-16. PMID: 10761354 Funding Source: Janssen Research Foundation; Stanley Foundation: NICHD Pediatric Pharmacology Research Unit.	RCT 10 wks 20 pts 5-15 yrs Conduct disorder	Adverse Events: AE / RIS / PBO / p Total / 80% / 40% Inc. appetite / 3 / 0 Sedation / 3 / 2 Headache / 1 / 1 Init. insomnia / 1 / 0 Restlessness / 2 / 0 Irritability / 1 / 0 Eruresis / 0 / 1 Nausea/vomiting / 1 / 1 Weight gain / 4.2 kg / .74kg / .003 Inc. prolactin / NM / NM EPS / 0 / 0 Lab / □ / □ ECG / □ / □ NM = not measured □□any changes not clinically significant 4 pts on RIS did not finish study: 3 withdrew due to lack of effectiveness 1 due to rash 7 pts on PBO did not finish study: 4 due to lack of benefit 2 due to noncompliance with study 1 lost to follow-up	RAAPP Significant Rating Scale/Subscale Changes Scale / RIS / PBO / p RAAP / -1.65 / -0.16 / 0.03 CGI -S / -2.58 / -0.08 / 0.003 CGI-I* / 1.80 / 3.60 / 0.002 CPRS Conduct Prob. / -28.0 / -1.75 / 0.0005 Psychosomatic / -13.7 / -2.1 / 0.04 Delinquent / -27.1 / 4.5 / 0.04 *Smaller score is better. On the other scales, a negative score denotes lessoning of symptoms. RAAPP = Rating of Aggression Against People and/or Property Scale CGI-S = Clinical Global Impression-Severity CGI-I = Clinical Global Impression-Improvement CPRS = Conners Parent Rating Scale	"These data provide preliminary evidence that risperidone may have efficacy in the treathment of youths with conduct disorder." (no page numbers on copy) Limitations: small sample size, brief length, high non-completion rate, no teacher ratings Comment: Paper is outside review timeframe (by2 months) but otherwise meets review criteria

Table C

Second Generation Antipsychotics (Atypical)

Olanzapine

Study & Funding source	Studies that met criteria	Safety	Efficacy	Conclusions Limitations Comments
Olanzapine (OLZ) Zyprexa® 36 PubMed citations, June 2, 2010 Search terms: clinical trial [PT] AND olanzapine AND (child OR adolescent) NOT adult	RCTs: 5 POLs: 4 (4 more RCTs and 8 other POLs in Antipsychotic Comparison section)	Adverse Effects: Appetite increase Weight gain Sedation GI disturbance Dizziness	FDA approved pediatric marketing indications: Schizophrenia 13-17 Bipolar I manic or mixed episodes 13-17	Weight gain is the single biggest issue in prescribing Olanzapine. It causes more weight gain than any other antipsychotic and therefore should generally not be the first medication used when medications are necessary.
Kryzhanovskaya L, Schulz SC, McDougle C, Frazier J, Dittmann R, Robertson-Plouch C, Bauer T, Xu W, Wang W, Carlson J, Tohen M. Olanzapine versus placebo in adolescents with schizophrenia: a 6-week, randomized, double-blind, placebo-controlled trial. J Am Acad Child Adolesc Psychiatry. 2009 Jan;48(1):60-70. PMID: 19057413 Funding Source: Eli Lilly and Company Study used in FDA approval process.	RCT 6 wks 107 13-17 Schizophrenia	Wt gain: O: 4.3 kg P: 0.1 kg p < .001 Significant increases in weight, triglycerides, uric acid, most liver function tests, & prolactin. EPS: No significant difference between OLZ and PBO.	Brief Psychiatric Rating Scale for Children OLZ; -19.4 PBO: -9.3 p = .003 ES = 0.63 Positive and Negative Symptom Scale OLZ: -21.3 PBO: -8.8 p = .005 ES = 0.6 Overt Aggression Scale OLZ: -0.9 PBO: -0.2 p = .051	"Olanzapine-treated adolescents with schizophrenia experienced significant symptom improvement." p. 60 This study showed less response and more adverse effects than adult studies of this med. Limitations: Short study with very strict inclusion criteria. May not predict response well in general youth SCZ population. Mildly ill patients were allowed to switch to the treatment arm at 3 weeks. This could bias study in favor of showing positive effect of olanzapine. Comments: . Multicenter study in US and Russia. It is possible that inclusion criteria differed. Childhood onset SCZ is known to be more severe than adult onset SCZ which can account for less positive response.
Hawkins KA, Keefe RS, Christensen BK, Addington J, Woods SW, Callahan J, Zipursky RB, Perkins DO, Tohen M, Breier A, McGlashan TH. Neuropsychological course in the prodrome and first episode of psychosis: findings from the PRIME North America Double Blind Treatment Study. Schizophr Res. 2008 Oct;105(1-3):1-9. Epub 2008 Sep 6. PMID: 18774696 Funding Source: Ely Lilly and Company	RCT 12 mos + 12 mos 60 pts Mean age 17.8 yrs SD = 4.8 yrs SCZ Prodrome (Similar to psychosis but with intact insight and no other diagnosis)	Not a focus of this study.	There was no significant effect of olanzapine on global neuropsychological status.	"The main finding is that neither treatment with olanzapine nor conversion to psychosis had a significant impact on neuropsychological functioning." p 7 "We found no evidence for a positive effect of olanzapine on neuropsychological functioning in the putative prodrome." "...our data do not support a neurocognitive rational for the antipsychotic treatment of the prodrome." Limitations: High attrition rate and small number in the olanzapine treated group that converted to psychosis. Comment: The basic assumption that overall neuropsychological function deteriorates prior to the onset of psychosis is not supported by this paper. Because of this, one would not expect to see a positive effect of olanzapine in this domain as it does not appear to be involved in onset of psychosis.

Table C

Second Generation Antipsychotics (Atypical)

Olanzapine

Study & Funding source	Studies that met criteria	Safety	Efficacy	Conclusions Limitations Comments
Tohen M, Kryzhanovskaya L, Carlson G, Delbello M, Wozniak J, Kowatch R, Wagner K, Findling R, Lin D, Robertson-Plouch C, Xu W, Dittmann RW, Biederman J. Olanzapine versus placebo in the treatment of adolescents with bipolar mania. Am J Psychiatry. 2007 Oct;164(10):1547-56. PMID: 17898346 Funding source: Eli Lilly and Company Study used in FDA approval process.	RCT 3 wks 161 pts 13-17 yrs Bipolar mania	Adaverse Events: Most common: Apetite increase Weight increase somnolence sedation Extrapyramidal Symptoms: No significant difference between OLZ and PBO. Weight change: OLZ: 3.7 kg PBO: 0.3 kg ≥7% weight increase OLZ: 41.9% PBO: 1.9%	Young Mania Rating Scale OLZ: -17.65 PBO: -9.99 $p < 0.001$ ES: 0.84 Met response criteria: OLZ: 44.8% PBO: 18.5% Met remission criteria: OLZ: 35.2% PBO: 11.1%	"Olanzapine was effective in the treatment of bipolar mania in adolescent patients. Patients treated with olanzapine, however, had significantly greater weight gain and increases in the levels of hepatic enzymes, prolactin, fasting glucose, fasting total cholesterol, and uric acid." Limitations: Short time length, patients had option to discontinue double blind condition to enter open label phase. Comment: Effect size is high and almost half of patients responded.
Hollander E, Wasserman S, Swanson EN, Chaplin W, Schapiro ML, Zagursky K, Novotny S. A double-blind placebo-controlled pilot study of olanzapine in childhood/adolescent pervasive developmental disorder. J Child Adolesc Psychopharmacol. 2006 Oct;16(5):541-8. PMID: 17069543 Funding Source: Lilly Research Laboratories	RCT 8 wks 11 6-14 yrs PDD's	Adverse Events: Mild Sedation common Mild Constipation No Extrapyramidal Symptoms experienced. Average Weight gain: OLZ: 7.5 lbs PBO: 1.5 lbs	Clinical Global Impression-Improvement: OLZ: 50% responders P:BO 20% responders Study did not show reduction of aggression, hyperactivity, or mood symptoms.	"Olanzapine may be a promising treatment for improving global functioning of PDDs, but the risk of significant weight gain remains a concern." Small heterogeneous sample size. Small heterogeneous sample size would probably not be able to show effects on aggression, hyperactivity or mood even if present.
McGlashan TH, Zipursky RB, Perkins D, Addington J, Miller T, Woods SW, Hawkins KA, Hoffman RE, Preda A, Epstein I, Addington D, Lindborg S, Trzaskoma Q, Tohen M, Breier A. Randomized, double-blind trial of olanzapine versus placebo in patients prodromally symptomatic for psychosis. Am J Psychiatry. 2006 May;163(5):790-9. PMID: 16648318 Funding Source: Ely Lilly and Company; NIMH; Tapscott Chair in Schizophrenia Studies at the University of Toronto	RCT 1 yr + 1 yr 60 pts 12 – 45 yrs Mean: 17.2 Median: 16 Psychosis prodrome (Similar to psychosis but less severe)	Adverse Events: Fatigue and wt gain were the most significant Wt gain: OLZ 8.79 kg P: 0.30 kg Extrapyramidal Symptoms: No difference during treatment phase	Scale of Prodromal Symptoms: OLZ: -6.73 PBO: -2.03 $p = .39$ Positive and Negative Symptom Scale Little change either group Montgomery Asberg Depression Rating Scale Little change either group Young Mania Rating Scale Little change either group	"...the primary objective of demonstrating a significant treatment difference in the rate of conversion to psychosis was not met...." Limitations: difficulty in identifying psychosis prodrome, difficulties in inter-rater reliability, lack of structured diagnostic assessment Comment: The difference in rates of conversion to frank psychosis was almost significant between the two groups, but study does NOT support treating the prodrome with OLZ. This study included older adolescents and adults which make the weight change less comparable to other studies which do not include older groups—especially for the placebo condition.

Table C

Second Generation Antipsychotics (Atypical)

Olanzapine

Study & Funding source	Studies that met criteria	Safety	Efficacy	Conclusions Limitations Comments
Fido A, Al-Saad S. Olanzapine in the treatment of behavioral problems associated with autism: an open-label trial in Kuwait. Med Princ Pract. 2008;17(5):415-8. Epub 2008 Aug 6. PMID: 18685284 Funding Source: Not stated in paper.	POL 13 wks 40 pts 7-17 yrs Autism	Adverse Events Extrapyramidal Symptoms: no change from baseline No significant enzyme or serum chemistry changes Weight gain: no significant change. 12% reported mild transient effects such as drowsiness or sedation. No subject withdrew from study for any reason.	Aberrant Behavior Checklist: (Efficacy = 25% reduction from baseline) Significant improvement (efficacy) in irritability, lethargy/withdrawal, stereotyped behavior, hyperactivity, and inappropriate speed. Clinical Global Impression-Severity of Illness Efficacy = 1 pt decrease 30% were considered much improved.	"Olanzapine was effective and well tolerated for the treatment of some behavioral symptoms (irritability, hyperactivity/noncompliance and lethargy/withdrawal) associated with autism." Limitations: Short study period, no control group Comments: Lack of weight gain, or other adverse events is notable in this POL.
Ross RG, Novins D, Farley GK, Adler LE. A 1-year open-label trial of olanzapine in school-age children with schizophrenia. J Child Adolesc Psychopharmacol. 2003 Fall;13(3):301-9. PMID: 14642018 Funding Source: Veteran's Administration Research Services; Eli Lilly and Company	POL 1 yr 20 pts 6-15 yrs SCZ or Schizoaffective disorder	Mean wt gain: 12.8 kg 4 dropped out due to wt gain Extrapyramidal Symptoms: no significant change Lab: no significant changes including serum glucose Sedation mentioned but not analyzed.	Measures of assessment: Brief Psychiatric Rating Scale for Children Scale for Assessment of Positive Symptoms Scale for Assessment of Negative Symptoms Responders = ≥ 20% symptom decrease and mild residual impairment. 6 wks: 68% 3 mos: 42% 1 yr: 74%	"Olanzapine appears useful in the treatment of childood-onset schizophrenia, although there may be a delayed onset of benefit for anxiety and negative symptoms. Weight gain is problematic, but the emergence of dyskinesias may be rare." Limitations: small sample size; only symptoms measured rather than functionality; open label; pts could take other medications Comments: This is a naturalistic study that closely mirrors conditions found in actual practice.
Frazier JA, Biederman J, Tohen M, Feldman PD, Jacobs TG, Toma V, Rater MA, Tarazi RA, Kim GS, Garfield SB, Sohma M, Gonzalez-Heydrich J, Risser RC, Nowlin Z A prospective open-label treatment trial of olanzapine monotherapy in children and adolescents with bipolar disorder. J Child Adolesc Psychopharmacol. 2001 Fall;11(3):239-50. PMID: 11642474 Funding Source: Eli Lilly and Compnay; NIMH	POL 8 wks 23 pts 5-14 yrs Bipolar disorder	Most common adverse events: Increased appetite Somnolence Abdominal pain Weight gain Weight gain: 5.0 kg, $p < 0.001$ Extrapyramidal Symptoms: no significant change I pt discontinued due to hospitalization for increased depression and suicidal ideation Lab: small but statistically significant changes in: CBC, ALT, pulse rate Prolactin: 6 cases asymptomatic hyperprolactinemia	Young Mania Rating Scale decrease (YMRS): -19.0, $p < 0.001$ Clinical Global Impression-Severity (CGI-S), mania 40% improvement; $p < 0.001$ Responders = YMRS ≥30% decline & CGI-S mania ≤3 Overall response rate: 61%	"Open label olanzapine treatment was efficacious and well tolerated in the treatment of acute mania in youths with bipolar disorder." p. 239 "Olanzapine monotherapy had beneficial effects on manic, depressive, psychotic, and aggressive symptoms in youths with acute BPD (manic type)." p. 248 Limitations: open label study Comment: Study used patients who had failed multiple previous medication trails, so the positive response is impressive.
Kemner C, Willemsen-Swinkels SH, de Jonge M, Tuynman-Qua H, van Engeland H. Open-label study of olanzapine in children with pervasive developmental disorder. J Clin Psychopharmacol. 2002 Oct;22(5):455-60. PMID: 12352267 Funding Source: Eli Lilly and Company	POL 3 mos 25 pt 6-16- yrs Autism or PDD NOS	Increased appetite Loss of strength Weight gain Weight gain mean: 5.8 kg Extrapyramidal Symptoms 3 children, resolved when dose lowered 2 pts withdrew for unknown or non-med reasons 1 other did not meet diagnostic criteria	Clinical Global Impression-Severity/Improvement: Only 3 responders by criteria of much improved or greater Aberrant Behavior Checklist: subscales for irritability, hyperactivity and excessive speech were significantly lower	"The weight gain and the arguably minimal clinically relevant effects of olanzapine may indicate that it has only limited use in the treatment of children with PDD." Limitations: open label, study group had higher than usual intellectual function for PDD'. Comment: Higher intellectual function of study subjects could bias the results against showing effectiveness of OLZ.

Table D

Second Generation Antipsychotics (Atypical)

Quetiapine

Study Funding source	Studies that Met Criteria	Safety	Efficacy	Conclusions, Limitations, Comments
Quetiapine (QTP) Generic Available Seroquel® 20 PubMed citations, June 3, 2010 Search terms: clinical trial [PT] AND olanzapine AND (child OR adolescent) NOT adult	RCTs: 4 + 1 post hoc study POLs: 3 (5 more POLs in Antipsychotic Comparison section)	Adverse Events GI upset Sedation Dizziness Fatigue Increased appetite Dry mouth Tachycardia Weight gain	FDA approved marketing indications: Schizophrenia 13-71 Bipolar mania 10-17	Past the FDA indications, literature supports use as adjunctive treatment in bipolar disorder. There are very few studies of QTP. QTP does not appear effective for treatment of depression in bipolar disorder and its use for aggression alone is equivocal. Weight gain is a problem but less so in patients receiving concomitant stimulant medication.
DelBello MP, Chang K, Welge JA, Adler CM, Rana M, Howe M, Bryan H, Vogel D, Sampang S, Delgado SV, Sorter M, Strakowski SM. A double-blind, placebo-controlled pilot study of quetiapine for depressed adolescents with bipolar disorder. Bipolar Disord. 2009 Aug;11(5):483-93. PMID: 19624387 Funding Source: AstraZeneca Pharmaceuticals.	RCT 8 wks 32 pts 12-18 yrs Depression in bipolar disorder	Adverse Effects / QTP / PBO / p GI upset / 65% / 33% / 0.16 Sedation / 59% / 33% / 0.18 Dizziness / 41% / 7% / 0.04 Cold symptoms / 24% / 20% / 1.0 Tooth pain / 18% / 0% / 0.23 Headaches / 18% / 33% / 0.42 Weight gain kg / +2.3 / +0.9 / 0.12 Inc. prolactin ng/ml / -2.47 / 0.05 / 0.3 Trig. mg/dL / +30 / -14 / 0.003 EPS / □ / □ / – Other Lab / □ / □ / – ECG / □□ / □□ / – Hypertension / 2 pts / 0 / – □= No significant between group difference in change □ = No clinical significance of changes Only dizziness showed a significant difference between QTP and PBO. 2 QTP pts developed hypertension. 1 pt left study due to suicide attempt, but remained on QTP and clinically improved.	Scale / QTP / PBO / p CDRS-R / -18.8 / -19.5 / 0.89 HAM-A / -4 / -5 / 0.74 YMRS / -5 / -4 / 0.76 CGI-BP-S / -1.8 / -1.6 / 0.9 CDRS-R = Chidren's Depression Rating Scale Revised HAM-A = Hamilton Anxiety Rating Scale CGI-BP-S = CGI Bipolar Version Severity	"The results suggest that quetiapine monotherapy is no more effective than placebo for the treatment of depression in adolescents with bipolar disorder " p. 483. Limitations: short length, small sample size Comment: This was not a study of manic symptoms and only applies to depression in bipolar disorder. High placebo response rate coupled with short length and small sample size may have precluded seeing any effect if present. Some adult stucies prior to this one had shown an effect for QTP on depression in bipolar disorder.

Table D

Second Generation Antipsychotics (Atypical)

Quetiapine

Study Funding source	Studies that Met Criteria	Safety	Efficacy	Conclusions, Limitations, Comments
Connor DF, McLaughlin TJ, Jeffers-Terry M. Randomized controlled pilot study of quetiapine in the treatment of adolescent conduct disorder. J Child Adolesc Psychopharmacol. 2008 Apr;18(2):140-56. PMID: 18439112 Funding Source: AstraZeneca Pharmaceuticals to D.F.C in part.	RCT 7 wks 19 pts 12-17 yrs Conduct Disorder	Adverse Effects / QTP / PBO / p Ave. # side effects / 6.1 / 8.9 / 0.12 Dec. mental alert.* / 33% / 90% / 0.01 Dec. emotional expression* / 11% / 70% / 0.009 Dec. facial expression* / 11% / 60% / 0.03 Weight gain kg / 2.3 / 1.1 / 0.46 Inc. prolactin ng/ml / +7.1 / +7.6 / 0.71 EPS, akathisia / 1 pt / 0 / -- Lab / - / - / -- ECG / NR / □□ / -- *Present more often in the PBO group. Others except EPS show no difference between groups. 1 pt on QTP developed akathisia. This patient had a history of head injury with loss of consciousness years prior to study.	Effectiveness Rating Scale Changes: Scale / QTP / PBO / p CGI-I / -2.5 / -0.5 / 0.007 OAS / -29.9 / +9.0 / 0.52 CPRS-CP Conduct Probs / -5.8 / +0.8 / 0.76 OAS = Overt aggression scale.	"Data from this methodologically controlled pilot study sugges: that quetiapine may be broadly beneficial in adolescents meeting diagnostic criteria for conduct disorder." ... "Quetiapine appears well tolerated." p. 153 Limitations: short length, small sample size, possible selection bias related to majority of adolescents offered participation declining to do so, randomized placebo group was older than QTP group Comment: QTP did not show an effect on aggression.
Barzman DH, DelBello MP, Adler CM, Stanford KE, Strakowski SM. The efficacy and tolerability of quetiapine versus divalproex for the treatment of impulsivity and reactive aggression in adolescents with co-occurring bipolar disorder and disruptive behavior disorder(s). J Child Adolesc Psychopharmacol. 2006 Dec;16(6):665-70. PMID: 17201610 Funding Source: AstraZeneca Pharmaceuticals.	"RCT" Post hoc 28 days 33 pts 12-18 yrs Impulsivity + Aggression in bipolar with disruptive behavior disorders	Adverse Events / QTP / DVP / p Total / NR / NR Sedation / 14 pts / 6 pts GI upset / 8 pts / 7 pts Headache / 8 pts / 4 pts Weight gain / NR / NR Inc. prolactin / NR / NR EPS / NR / NR Lab / □ / □ ECG / □ / □ NR = Not Reported □ = No clinical significance of changes No subject discontinued due to medication or Adverse Event.	Rating Scale Improvement Scale / QTP / DVP / ES PANSS -Excited Comp. / -8.0* / -7.3* / 0.1 * p < 0.0001 for within treatment group PANSS = Positive & Negative Symptom Scale	"Quetiapine and divalproex showed similar efficacy for the treatment of impulsivity and reactive aggression related to co-occurring bipolar and disruptive behavior disorders in adolescents. Quetiapine and divalproex are both useful as monotherapy ..." p. 665. Limitations: post hoc, small sample size, short length, hospitalized pts

Table D

Second Generation Antipsychotics (Atypical)

Quetiapine

Study Funding source	Studies that Met Criteria	Safety	Efficacy	Conclusions, Limitations, Comments
DelBello MP, Kowatch RA, Adler CM, Stanford KE, Welge JA, Barzman DH, Nelson E, Strakowski SM. A double-blind randomized pilot study comparing quetiapine and divalproex for adolescent mania. J Am Acad Child Adolesc Psychiatry. 2006 Mar;45(3):305-13. PMID: 16540815 Funding Source: AstraZeneca.	RCT 28 days 50 pts 12-18 yrs Bipolar I mania	Adverse Events / QTP / DVP / p Total: □ / □ Sedation: 60% / 36% / 0.2 Dizziness: 36% / 36% / 1.0 GI upset: 24% / 28% / 1.0 Dry mouth: 24% / 8% / 0.3 Inc. appetite: 8% / 12Y / 1.0 Prolactin: NR / NR / -- Other Lab: □ / □ / – Weight gain kg: 4.4 / 3.6 / -- EPS: □ / □ / – Akathisia: □ / □ / – ECG: □ / □ / – □ = No significant between group difference in change □ = No clinical significance of changes 1 Serious AE: a pt in DVP group was rehospitalized due to symptom exacerbation and withdrew from the study.	Rating Scale Change/Improvement Scale / QTP / DVP / ES or p YMRS: -23* / -19* / ES =0.28 -Remission: 60% / 28% / p = 0.02 CDRS: -21* / -22* / ES =0.09 CGI-BP-Is 2 -Overall: 72% / 40% / p = 0.02 -Manic: 84% / 56% / p = 0.03 * p < 0.0001 for within treatment group YMRS = Young Mania Rating Scale CDRS = Children's Depression Rating Scale CGI-BP = Clinical Global Impression-Bipolar Improvement occurred more rapidly in QTP group. 2 pts in DVP group discontinued due to lack of efficacy.	"The results suggest that quetiapine is at least as effective as divalproex in the teatment of acute manic symptoms as-sociated with adolescent bipolar disorder; however, a quicker reduction of manic symptoms may occur with quetiapine as compared with divalproex." p. 305. Limitations: small sample size, short length, no placebo control, hospitalize patients Comment:
Delbello MP, Schwiers ML, Rosenberg HL, Strakowski SM. A double-blind, randomized, placebo-controlled study of quetiapine as adjunctive treatment for adolescent mania. J Am Acad Child Adolesc Psychiatry. 2002 Oct;41(10):1216-23. PMID: 12364843 Funding Source: AstraZeneca Pharmaceuticals.	RCT 6 wks 30 pts 12-18 yrs Mania	Adverse Events / DVP + PBO / DVP+QTP Total Sedation: 33% / 80% Nausea/vomiting: 40% / 27% Dizziness: 20% / 33% Headache: 47% / 47% GI irritation: 33% / 47% wt gain: +2.5 kg / +4.2 kg prolactin ng/m/: -5.7 / -1.6 Other Lab: □ / □ EPS: □ / □ Lab: □ / □ ECG: □ / □ □= No significant between group difference in change □No clinical significance of changes No subject developed serious AE. No significant differences between DVP + PBO and DVP + QTP.	Rating Scale Change/Response Rate Scale / DVP + PBO / DVP + QTP / p YMRS: ~ -13 / ~ -20 / 0.3 ≥ 50% reduction: 53% / 87% / 0.5 CDRS: NR / NR / □ PANSS: NR / NR / □ CGAS: NR / NR / □ □No significant difference in improvement YMRS = Young Mania Rating Scale CDRS = Children's Depression Rating Scale PANSS = Positive & Negative Symptom Scale CGAS = Children's Global Assessment Scale	"The findings of this study indicate that quetiapine in combination with DVP is more effective for the treatment of adolescent bipolar mania than DVP alone. In addition, the results suggest that quetiapine is well tolerated when used in combination with DVP for the treatment of mania." (No page numbers on copy.) Limitations: Comment:
Schimmelmann BG, Mehler-Wex C, Lambert M, Schulze-zur-Wiesch C, Koch E, Flechtner HH, Gierow B, Maier J, Meyer E, Schulte-Markwort M. A prospective 12-week study of quetiapine in adolescents with schizophrenia spectrum disorders. J Child Adolesc Psychopharmacol. 2007 Dec;17(6):768-78. PMID: 18315449 Funding Source: AstraZeneca	POL 12 wks 56 pts 12-17 yrs SCZ Spectrum	Adverse Events / QTP Total: 78.6% Somnolence: 21.4% Fatigue: 17.9% Headache: 17.9% Sexual symptoms: 11 pts Thyroxine ng/dl: -2.5 Inc. prolactin: □ Other Lab: □ Weight gain: +6.2 kg Extrapyramidal s.: 8.9% Akathisia: 3.6% ECG: □ 1 pt discontinued due to adverse event	Effectiveness Rating Scale Changes: Scale / QTP / ES PANSS Total: -24.9 / 0.92 -Positive: -6.9 / 0.91 -Negative: -4.6 / 0.50 -Disorganization: -5.5 / 1.01 -Impulsivity/Hostility: -2.3 / 0.48 -Anxiety/Depression: -4.3 / 0.97 CGI -Severity of illness: -1.5 / NA -Global improvement: 2.6 / NA 30% discontinued due to lack of effectiveness 34.6% responded (≥50% decrease PANSS) PANSS = Positive & Negative Symptom Scale	"In this sample of mostly drug-naïve patients with early-onset schizophrenia spectrum disorders, significant reductions in PANSS total and positive scores were detected....The significant weight gain with its potentially severe medical consequences must be weighed against quetiapine's effectiveness." p. 269. Limitations: open label, no randomization, no control group, no interrater reliability assessments, high drop-out rate, small sample size Comment: Most pts who achieved response showed improvement in the first week of treatment.

Table D

Second Generation Antipsychotics (Atypical)

Quetiapine

Study Funding source	Studies that Met Criteria	Safety	Efficacy	Conclusions, Limitations, Comments
Kronenberger WG, Giauque AL, Lafata DE, Bohnstedt BN, Maxey LE, Dunn DW. Quetiapine addition in methylphenidate treatment-resistant adolescents with comorbid ADHD, conduct/oppositional-defiant disorder, and aggression: a prospective, open-label study. J Child Adolesc Psychopharmacol. 2007 Jun;17(3):334-47. PMID: 17630867 Funding Source: AstraZeneca Pharmaceuticals LP.	POL 14 wks 24 pts 12-16 yrs ADHD and severe aggression	Common Adverse Events: Adverse Events — MPH — MPH +QTP Total — 79% — 96% Headache — 33% — 17% Insomnia — 29% — NR Stomachache/nausea — 25% — 29% Dec. appetite — 21% — 17% Fatigue/sedation — 17% — 50% Upper respiratory — 13% — 38% Flu-like syndrome — NR — 21% Vomiting — NR — 17% Weight gain kg — –0.9 — +1.2 Inc. prolactin — NR — NR EPS — 0 — 0 Lab — □ — □ ECG — □ — □ □ = No clinical significance of changes Discontinuations due to AE: 3 in MPH + QTP phase (sedation, agitation). Weight loss due to MPH, regained with QTP.	Effectiveness Rating Scale Changes at end of MPH monotherapy and further change at end of MPH + QTP treatment: Scale — MPH — p — MPH + QTP — p CGI-S — -1.2 — < .001 — -1.3 — < .001 RAAP — -1.1 — < .001 — -1.2 — < .001 ADHD-RS — -13.0 — <.001 — -8.0 — < .001 CGI-S = Clinical Global Impression-Severity RAAPP = Rating of Aggression Against People and/or Property ADHD-RS = ADHD Rating Scale	"Quetiapine addition to methyphenidate was effective in reducing ADHD and aggression in individuals who did not respond sufficiently...to OROS methylphenidate alone at a 54 mg/day dase." p. 334 Limitations: no analysis of prior psychotherapy treatment, open label, short length, small sample size Comment: QTP effectiveness was in addition to what was first achieved with MPH alone. Both decreased symptoms of aggression and ADHD.
DelBello MP, Adler CM, Whitsel RM, Stanford KE, Strakowski SM. A 12-week single-blind trial of quetiapine for the treatment of mood symptoms in adolescents at high risk for developing bipolar I disorder. J Clin Psychiatry. 2007 May;68(5):789-95. PMID: 17503991 Funding Source: Stanley Medical Research Institute; AstraZeneca Pharmaceuticals LP, Wilmington, Del.	POL 12 wks 20 pts 12-18 yrs Mood Symptoms (but not meeting criteria for Bipolar I + relative with Bipolar disorder)	Adverse Events — QTP — p Total — NR — Somnolence — 55% — Headache — 25% — Musculoskeletal pain — 25% — Dyspepsia — 25% — Weight gain kg — +3.8 — < 0.0001 Inc. prolactin — □ — EPS — □ — Lab — □ — ECG — □ — □ =No clinical significance of changes No subject discontinued due to Adverse Events. No serious Adverse Events occurred.	Rating Scale Improvement or Change Scale — QTP — p CGI-I ≤ 2 — 87% — YMRS — -9.4 — < 0.0001 CDRS-R — -10.5 — 0.0003 CGI-I = Clinical Global Impression-Improvement YMRS = Young Mania Rating Scale CDRS-R = Children's Depression Rating Scale-Revised	"Although these findings are limited by the small sample size and open-label treatment, the results suggest that quetiapine may be an effective treatment for mood symptoms in adolescents with a familial risk for developing bipolar I disorder." p. 789. Limitations: small sample size, open label, heterogeneous diagnoses, genetic heterogeneity, short length

Table E

Second Generation Antipsychotics (Atypical)

Ziprasidone

Study & Funding source	Studies that met criteria	Safety	Efficacy	Conclusions, Limitations, Comments
Ziprasidone (ZIP) Generic available Geodon® 5 PubMed citations, June 5,2010 Search terms: clinical trials [PT] AND ziprasidone AND (child OR adolescent) NOT adult	RCTs: 1* (*Out of review time frame by 2 months) POLs: 2	Adverse effects: Lethargy Drowsiness Agitation Tachycardia Cardiac conduction slowing (lengthens QTc interval)	No FDA approved pediatric marketing indications.	Greatest QTC prolongation of atypicals Less risk for weight gain. "At present, ziprasidone should be considered a second or third-line option for a limited set of conditions. A role may exist for ziprasidone in patients who have experienced significant metabolic adverse effects with other atypical antipsychotics." p. 220 [ZIP0a] Very little evidence is available for review.
Sallee FR, Kurlan R, Goetz CG, Singer H, Scahill L, Law G, Dittman VM, Chappell PB. Ziprasidone treatment of children and adolescents with Tourette's syndrome: a pilot study. J Am Acad Child Adolesc Psychiatry. 2000 Mar;39(3):292-9. PMID: 10714048 Abstract Funding Source: Unknown	RCT 8 wks 28 pts 7-17 yrs Tic Disorders	Most commone adverse event: Transient somnolence No clinically significant effects on ratings of extrapyramidal symptoms, akathisia, or tardive dyskinesia	Yale Global Tic Severity Scale subscale changes Global Severity: Reduction with ZIP > PBO p = 0.016 Severity Reduction with ZIP > PBO p = 0.008	"In this limited sample, ziprasidone (5-40 mg/day) appears to be effective and well tolerated in the treatment of Tourette's syndrome. Ziprasidone may be associated with a lower risk of extrapyramidal side effects in children with tic disorders." Abstract Limitations: small samle size, heterogeneous diagnostic group, short length Comment: Paper is just before review time period and is only RCT available to review. Reviewed in abstract only. No data on cardiac function mentioned.
DelBello MP, Versavel M, Ice K, Keller D, Miceli J. Tolerability of oral ziprasidone in children and adolescents with bipolar mania, schizophrenia, or schizoaffective disorder. J Child Adolesc Psychopharmacol. 2008 Oct;18(5):491-9. PMID: 18928413 Funding Source: Pfizer Inc.	POL 3 wks + 6 mos 63 pts 10-17 yrs Bipolar mania, SCZ, or schizoaffective disorder	Adverse Events (AEs) — Low dose / High dose Total 91% / 95% Sedation 21.7% / 37.5% Somnolence 34.8% / 27.5% Nausea 21.7% / 27.5% Headache 13.0% / 27.5% Vomiting 13.0% / 20.0% ≥ 7% wt gain 13.0% / 2.5% Adverse Events — Period 1 / Period 2 Inc. prolactin 4 pts / 9 pts EPS □□ / □ Lab Ø / Ø ECG Ø / 1 QTC inc. 13% discontinued on low dose in Period 1 due to AEs. 40% discontinued on high dose in Period 1 due to AEs. 20% discontinued in Period 2 (next 6 mos) due to AEs. Serious AEs were suggestive of poor symptom control.	Rating Scale Changes for pts who completed end of Period 1 Scale — Low Dose — ES — High Dose — ES YMRS --BP -17.2 2.1 -13.1 1.47 BPRS-A --SCZ/A -9.5 2.0 -15.2 4.75 CGI-S --BP -1.6 1.14 -1.7 1.42 --SCZ/A -0.7 0.89 -0.8 1.60 YMRS = Young Mania Rating Scale BPRS-A = Brief Psychiatric Rating Scale CGI-S = Clinical Global Impression-Severity BP = Pts with bipolar disorder SCZ/A = Pts with schizophrenia or schizoaffective disorder	"No unexpected tolerability findings were observed in this prospective trial of zipasidone in children and adolescents with bipolar mania, schizaphrenia, or schizoaffective disorder." p. 491. "Ziprasidone produced clinically meaningful symptomatic changes in subjects with bipolar disorder or schizophrenia/schizoaffective disorder..." p. 497. Limitations: open label, included high fixed doses in Period 1, small sample size, lack of control group Comment: High fixed dosages in one group in Period One may have increased Adverse Eeffects over what would be seen in regular clinical practice. This paper was not primarily a study of efficacy.

Table E

Second Generation Antipsychotics (Atypical)

Ziprasidone

Study & Funding source	Studies that met criteria	Safety	Efficacy	Conclusions, Limitations, Comments
Blair J, Scahill L, State M, Martin A. Electrocardiographic changes in children and adolescents treated with ziprasidone: a prospective study. J Am Acad Child Adolesc Psychiatry. 2005 Jan;44(1):73-9. PMID: 15608546 Funding Source:	POL 6 mos 20 pts 7-18 yrs Pediatric outpts taking ziprazidone	Significant changes in HR, PR interval, QTc interval, but not in QRS complex width Mean QTc prolongation: 28 milliseconds (longer than in adults) QTc of > 440 milliseconds has been a generally accepted cut-off for normal, above which concern might be appropriate. 3 pts in this study reached or exceeded 450 millisec at least 1x Significant dose dependence not demonstrated. Automated ECG readings will miss many QTc prolongations.	Efficacy not assessed in this paper.	"These preliminary findings, occurring at doses low by current treatment standards, suggest that close electrocardiographic monitoring is warranted when prescribing ziprasidone to children, particularly at higher doses or when combined with other QTc-prolonging agents." (No page numbers on copy.) Limitations: small sample size, lack of placebo control, open label, unbalanced gender ration, heterogeneous ages and diagnoses, premature discontinuation

Table F

Second Generation Antipsychotics (Atypical)

Aripiprazole

Study & Funding source	Criteria	Safety	Efficacy	Conclusions, Limitations, Comments
Aripiprazole (ARI). Abilify® 17 PubMed citations, June 2, 2010 Search terms: clinical trial [PT] AND aripiprazole AND (child OR adolescent) NOT adult	RCTs: 5 (papers 6) POL: 3 (1 more POL in Antipsychotic Comparison section)	Most frequent Adverse Events: Extrapyramidal symptoms Somnolence Akathisia Headache Tremor Dizziness	FDA approved pediatric marketing indications: Schizophrenia in (13-17 yrs) Mania or mixed episodes in bipolar d. (10-17 yrs) Irritability in autism (6-17 yrs)	"Form the available evidence, use of aripiprazole could be justified in Bipolar Disorder (manic or mixed episodes) and Schizophrenia, both of which are FDA approved indications in the child and adolescent population." [p. no page numbers available, ARI10] Weight gain not an issue. Does not raise prolactin levels.
Robb AS, Carson WH, Nyilas M, Ali M, Forbes RA, Iwamoto T, Assunção-Talbott S, Whitehead R, Pikalov A. Changes in positive and negative syndrome scale-derived hostility factor in adolescents with schizophrenia treated with aripiprazole: post hoc analysis of randomized clinical trial data. J Child Adolesc Psychopharmacol. 2010 Feb;20(1):33-8. PMID: 20166794 Funding Source: Otsuka Pharmaceutical Co., Ltd.	RCT "Post hoc" 6 wks 302 pts 13-17 yrs Schizophrenia	Not Addressed.	Positive & Negative Symptom Scale-Hostility Factor change: ARI 10 mg: -3.0 ARI 30 mg: -3.7 PBO: -2.1	Conclusion: "This post hoc analysis shows that aripiprazole (10 and 30 mg/day) is an effective treatment for hostility symptoms in adolescents with schizophrenia." p. 33 Limitations: post hoc, fixed dose, study not originally designed to study hostility, no analysis of possible contributing factors Comment: Findings mirror those in adult studies
Owen R, Sikich L, Marcus RN, Corey-Lisle P, Manos G, McQuade RD, Carson WH, Findling RL. Aripiprazole in the treatment of irritability in children and adolescents with autistic disorder. Pediatrics. 2009 Dec;120(6):1533-1540. Funding Source: Bristol-Myers Squibb and Otsuka Pharmaceutical All authors but 2 employed by industry. Study used in FDA approval process.	RCT 8 wks 98 6-17 yrs Autism with tantrums, aggression, and/or self-injurious behavior	Most common Adveres Events: fatigue, somnolence No serious Adevers Events reported. Extrapyrmidal Symptoms: ARI: 14.9% PBO: 8.0% Mean weight gain: ARI: 2.0 kg PBO: 0.8 kg Discontinuation rates due adv events: ARI: 10.6% PBO: 5.9%	Aberrant Behavior Checklist-Irritability mean decrease: (- score denotes improvement) ARI: -12.9 PBO: -5.0 p < .001 Clinical Global Impression-Improvement mean rating at week 8: "aripirazole showed statistically significantly greater improvement" p < .001	Conclusion: "During an 8-week period, aripiprazole was efficacious and generally well tolerated in the treatment of irritability associated with autistic disorder in children and adolescents who may be experiencing tantrums, aggression, self-injurious behavior, or a combination of these symptoms." Limitations: Study used flexible 2, 5, and 10 mg dosages of aripiprazole.
Marcus RN, Owen R, Kamen L, Manos G, McQuade RD, Carson WH, Aman MG. A placebo-controlled, fixed-dose study of aripiprazole in children and adolescents with irritability associated with autistic disorder. J Am Acad Child Adolesc Psychiatry. 2009 Nov;48(11):1110-9. Funding Source: Bristol-Myers Squibb and Otsuka Pharmaceutical All authors but one employed by industry. Study used in FDA approval process.	RCT 8 wks 218 6-17 yrs Autism with tantrums, aggression, and/or self-injurious behavior	Discontinuation rates due to adverse events: ARI 5mg: 9.4% ARI 10mg: 13.6% ARI 15mg: 7.4% PBO: 7.7% Most common event leading to discontinuation was sedation. 2 serious adverse events: ARI 5mg: pre-syncope; ARI 10mg: aggression Mean weight gain: ARI 5mg: +1.5 kg ARI 10mg: +1.3 kg ARI 15mg: +1.5 PBO: 0.3kg p < .05 versus placebo	Aberrant Behavior Checklist-Irritability: (- score denotes improvement) ARI 5mg: -12.4 ARI 10mg: -13.2 ARI 15mg: -14.4 PBO: -8.4 Clinical Global Impression-Irritability mean rating at 8 week endpoint: All dosages showed significantly greater improvement compared to placebo.	Conclusion: "Aripiprazole was efficacious and generally safe and well tolerated in the treatment of children and adolescents with irritability associated with autistic disorder." Limitations: Study limited to autistic patients with irritability, moltiple fibbed-dose design, short term

Table F

Second Generation Antipsychotics (Atypical)

Aripiprazole

Study & Funding source	Criteria	Safety	Efficacy	Conclusions, Limitations, Comments
Findling RL, Nyilas M, Forbes RA, McQuade RD, Jin N, Iwamoto T, Ivanova S, Carson WH, Chang K. Acute treatment of pediatric bipolar I disorder, manic or mixed episode, with aripiprazole: a randomized, double-blind, placebo-controlled study. J Clin Psychiatry. 2009 Oct;70(10):1441-51. Funding Source: Otsuka Pharmaceutical All authors but two employed by industry. Study used in FDA approval process.	RCT 4 wks 296 10-17 yrs Pediatric Bipolar I Disorder, manic or mixed, with or without psychosis	Most common adverse events: Extrapyramidal symptoms, somnolence: ARI 30 mg < ARI 10mg Average weight gain: ARI 10mg: 0.82 kg (p = .35) ARI 30mg: 1.08 kg (p = .13) PBO: 0.56 kg Not significantly different	Young Mania Rating Scale starting score ≥ 20 with ≥ 50% reduction defined as response. Percent that responded: ARI 10mg: 44.8% ARI 30mg: 63.6% PBO: 26.1% p < .01 for both doses Improvement in mania reflected in Clinical Global Impression-Bipolar (CGI-BP) scores for mania and General Behavior Inventory (GBI) scores by caregivers and subjects CGI-BP and GBI scores for depression do NOT show improvement	"Aripiprazole in daily doses of 10 mg or 30 mg is an effective and generally well-tolerated acute treatment for pediatric subjects with bipolar I mania or mixed episodes." p. 1441 "Data supporting the use of aripiprazole as an adjunct to antidepressant therapy in adults with major depressive disorder should not be extrapolated to this pediatric population." Limitations: short term, some missing clinical information, no active comparison group Comment: This study has a subsequent long-term extension phase that is not yet published.
Tramontina S, Zeni CP, Ketzer CR, Pheula GF, Narvaez J, Rohde LA. Aripiprazole in children and adolescents with bipolar disorder comorbid with attention-deficit/hyperactivity disorder: a pilot randomized clinical trial. J Clin Psychiatry. 2009 May;70(5):756-64. PMID: 19389329 Funding Source: Conselho Nacional de Desenvolvimento Cientifico e Tecnologico; Bristol Myers Squibb.	RCT 6 wks 43 pts 8-17 yrs Bipolar Disorder with co-morbid ADHD	Wt gain: ARI: +1.2 kg PBO: +0.72 kg ES: 0.35 No significant difference. Adverse events count: ARI: 3.76 PBO: 4.83 No significant difference.	Young Mania Rating Scale (YMRS) scores: ARI: -27.22 PBO: -19.52 ES: 0.80 Swanson, Nolan, & Pelham Scale-IV scores: ARI: -0.79 PBO: -0.55 No significant difference. Response (≥ 50% in YMRS): ARI: 88.9% PBO: 52% Remission Young Mania Rating Scale (≤12): ARI: 72% PBO: 32%	"Aripiprazole was effective in reducing manic symptoms and improving global functioning without promoting severe adverse events or weight gain. No significant treatment effect in AHDH symptoms was observed." p. 756 Limitations: small sample size, no correction for multiple comparisons, heterogeneity of developmental level, all assessments by only the principal investigator Comment: Bipolar disorder and ADHD are frequently diagnosed as co-morbid, so this study is very practical for clinical care.
Findling RL, Robb A, Nyilas M, Forbes RA, Jin N, Ivanova S, Marcus R, McQuade RD, Iwamoto T, Carson WH. A multiple-center, randomized, double-blind, placebo-controlled study of oral aripiprazole for treatment of adolescents with schizophrenia. Am J Psychiatry. 2008 Nov;165(11):1432-41. Epub 2008 Sep 2. PMID: 18765484 Funding Source: Otsuka Pharmaceutical Co., Ltd. Study used in FDA approval process.	RCT 6 wks 302 pts 13-17 yrs Schizophrenia	Common Adverse Events: Extrapyramidal symptoms (1 study dropout) Somnolence Tremor Weight gain: ARI 10 mg: 0.0 kg ARI 30 mg: 0.2 kg PBO: -0.8 kg Prolactin in ng/ml ARI 10 mg: -11.93 ARI 30 mg: -15.14 P: -8.45 No clinically relevant changes in cardiac status	Positive & Negative Symptom Scale total change: ARI 10 mg: -26.7 p = 0.002 ARI 30mg: -28.6 p = 0.0002 PBO: -21.2 Clinical Global Impression-Improvement ARI 10 mg: 2.7 p = 0.002 ARI 30 mg: 2.5 p = 0.008 PBO: 3.1	"Both 10- and 30-mg/day doses of aripiprazole were superior to placebo in the acute treatment of adolescent schizophrenia." 4. 1432 On the PANSS negative subscale, ARI at 30 mg does separate out as superior to placebo at the end of the study. Lower dosing may be more appropriate. Limitations: short study length, only applies to adolescents with SCZ Comments: This study attempted to address short-comings of other ARI studies, by being RCT with large sample size. This RCT shows a very large placebo response, which should be considered when interpreting the POL studies for this medication.

Table F

Second Generation Antipsychotics (Atypical)

Aripiprazole

Study & Funding source	Criteria	Safety	Efficacy	Conclusions, Limitations, Comments
Findling RL, Kauffman R, Sallee FR, Salazar DE, Sahasrabudhe V, Kollia G, Kornhauser DM, Vachharajani NN, Assuncao-Talbott S, Mallikaarjun S, Iwamoto T, McQuade RD, Boulton DW, Blumer J. An open-label study of aripiprazole: pharmacokinetics, tolerability, and effectiveness in children and adolescents with conduct disorder. J Child Adolesc Psychopharmacol. 2009 Aug;19(4):431-9. PMID: 19702495 Funding Source: Not stated but presumably industry. All authors but 4 employed by industry.	POL 14d and 36 mo 12 pts 6-12 yrs 11 pts 13-17 yrs Conduct Disorder with aggression	Adverse events: Mild extrapyramidal symptoms Child: 2 at 14 d, 1 in 36 mo Adolescent: 1 in Phase A, 1 in Phase B No serious AE's No discontinuations due to AE's No prolactin abnormalities No clinically significant vital sign abnormalities Mean wt change at 36 mo Child: +9.0 kg Adolescent: 13.3 kg	Rating of Aggression Against People and/or Property score improvement Child: -0.82 at 14 d -1.00 at 36 mo Adolescent: -1.00 at 14 d -0.75 at 36 mo Clinical Global Impression score much or very much improved: Child: 63.6% at 14 d 66.67% at 36 mo Adolescent: 45.5% at 14 d 100% at 36 mo	Conclusions: "Preliminary data suggest that aripiprazole may improve symptoms of CD with modest impact on cognitive function in both children and adolescents; however, the sample size is too small to draw any firm conclusions." p. 437 "Aripiprazole appeared to be safe and generally well tolerated by pediatric patients when appropriate dosing was used." p. 438 Limitations: Small sample size, open label, no control, comorbid ADHD allowed Comment: This is the first study conducted in children; it was conducted before commercial release of aripiprazole. Its purpose was to determine dosing and explore efficacy and safety.
Stigler KA, Diener JT, Kohn AE, Li L, Erickson CA, Posey DJ, McDougle CJ. Aripiprazole in pervasive developmental disorder not otherwise specified and Asperger's disorder: a 14-week, prospective, open-label study. J Child Adolesc Psychopharmacol. 2009 Jun;19(3):265-74. PMID: 19519261 Funding Source: AACAP, Daniel X. and Mary Freedman Fellowship; Bristol-Myers Squibb Co.; NIH; NIMH	POL 14 wks 25 pts 5-17 yrs PDD-NOS or Asperger's disorder	Mild extrapyramidal symptoms Weight gain: 2.7 kg Basal Metabolic Index (BMI): 21.1 (change: = +0.8) p ≤□ BMI z score change: +0.26 (Less than proposed sig. z score change of 0.5) No significant cardiac changes Prolactin change: -6.4 p ≤ 1 □□pt withdrew due to Adverse Event.	Clinical Global Impression-Improvement (CGI-I) 1.6 p ≤ 0.0001 Aberrant Behavior Checklist-Irritability (ABC-I) change -20.9 p ≤ 0.001 Responders: (CGI-I of much/very much improved and □25% improvement ABC-I) 88%	"These preliminary data suggest that aripiprazole may be effective and well tolerated for severe irritability in pediatric patients with PDD-NOS or Asperger's disorder." p. 265 Limitations: small sample size, very small sample size for Asperger's subset Comment: Medications in general have not been shown to effect the core social symptoms of PDD spectrum; however there is some evidence that ARI may have directly positively affected this deficit in this study.
Yoo HK, Choi SH, Park S, Wang HR, Hong JP, Kim CY. An open-label study of the efficacy and tolerability of aripiprazole for children and adolescents with tic disorders. J Clin Psychiatry. 2007 Jul;68(7):1088-93. PMID: 17685747 Funding Source: None stated.	POL 8 wks 24 pts 7-18 yrs Tic Disorders	Most common adverse events: Sedation 37.5% Nausea 20.8% Headache 16.6% 58% experienced 1 or more adverse effects 25% of pts discontinued ARI due to intolerable adverse effects Extrapyramidal symptoms: 8.3 % Akathisia: 8.3% Height/Weigh: no significant changes Lab: no significant changes ECG: no significant changes	Yale Global Tic Severity Scale change: -14.1 p < 0.001 Mean reduction: 52.8% Clinical Global Impression-Improvement much/very much improved: 79.2%	"This open-label study suggests that aripiprazole is an efficacious and safe treatment for children and adolescents with tic disorders." p. 1088 Limitations: Small sample size, short length, open label, lack of control group Comment: ARI may be more effective at tic reduction than other SGA's although perhaps still less so than FGA's—Haldol and Pimozide.

Table G

Second Generation Antipsychotics (Atypical)

Other Second Generation Antipsychotics

Drug	References	Met Criteria	Safety	Efficacy	Conclusion, Limitations, Comments
Iloperidone Fanapt®	7 citations NLM gateway May 24, 2010 Search terms: Clinical trial [PT] AND iloperidone AND (child OR adolescent) NOT adult	None	No data No clinical trial data.	No FDA pediatric marketing indications. No clinical trial data.	Insufficient evidence to draw any conclusions.
Paliperidone invega®	4 citations NLM gateway July 5, 2010 Search terms: Clinical trial [PT] AND paliperidone AND (child OR adolescent) NOT adult	None	No data No clinical trial data.	No FDA pediatric marketing indications. No clinical trial data.	Insufficient evidence to draw any conclusions.
Asenapine Sahpris®	0 citations NLM gateway July 5, 2010 Search terms: Clinical trial [PT] AND asenapine AND (child OR adolescent) NOT adult	NA	No data No clinical trial data.	No FDA pediatric marketing indications. No clinical trial data.	Insufficient evidence to draw any conclusions.

Table H

Typical Antipsychotics

First Generation Antipsychotics

Drug	References	Met Criteria	Safety	Efficacy	Conclusions, Limitations, Comments
Chlorpromazine Generic available (Thorazine® no longer available)	1 PubMed citations, June 2, 2010 Search terms: clinical trial [PT] AND chlorpromazine AND (child OR adolescent) NOT adult	None	No recent data.	For ages 6 mos+ Nausea and vomiting Presurgical apprehension Severe behavioral problems Hyperactivity with impulsivity, inattention, aggression, mood lability, and/or poor frustration tolerance The following statement appears in the FDA approved package insert: "Chlorpromazine should generally not be used in pediatric patients under 6 months of age except where potentially lifesaving. It should not be used in conditions for which specific pediatric dosages have not been established." [1]	No clinical trials in the last 10 years meet criteria.
Haloperidol Generic available Haldol®	13 PubMed citations, June 2, 2010 Search terms: clinical trial [PT] AND haloperidol AND (child OR adolescent) NOT adult	RCTs: 2 POLs: 2	See Antipsychotic Comparison Table I	For Ages 3+: Psychotic disorders Tourette's disorder (tics) Severe behavioral problems Hyperactivity with impulsivity, inattention, aggression, mood lability, and/or poor frustration tolerance	4 clinical trials in the last 10 years meet criteria and are listed under Medication Comparison Studies
Molindone Moban®	1 PubMed citations, June 2, 2010 Search terms: clinical trial [PT] AND molindone AND (child OR adolescent) NOT adult	RCTs: 1	See Antipsychotic Comparison Table I	No FDA approved pediatric marketing indications. However the following statement appears implying tacit approval of marketing above age 12: "Use of MOBAN in pediatric patients below the age of twelve years is not recommended because safe and effective conditions for its usage have not been established." [1]	1 clinical trial in the last 10 years meets criteria and is listed under Medication Comparison Studies. **DISCONTINUED 1-13-10** **Supplies expected to be depleted as of 6-30-10.**
Perphenazine Generic Available Trilafon	5 PubMed citations, June 2, 2010 Search terms: clinical trial [PT] AND perphenazine AND (child OR adolescent) NOT adult	None	No recent data.	No FDA approved pediatric marketing indications.	No studies in the last 10 years meet criteria.
Pimozide Orap®	2 PubMed citations, June 2, 2010 Search terms: clinical trial [PT] AND pimozide AND (child OR adolescent) NOT adult	RCTs: 1	See Antipsychotic Comparison Table I	No FDA approved pediatric marketing indications. However the following pediatric use guidelines are given: "Pediatric Use Although Tourette's Disorder most often has its onset between the ages of 2 and 15 years, information on the use and efficacy of ORAP in patients less than 12 years of ages is limited. A 24-week open label study in 36 children between the ages of 2 and 12 demonstrated that pimozide has a similar safety profile in this age group as in older patients and there were no safety findings that would preclude its use in this age group."[2]	1 clinical trial in the last 10 years meets criteria and is listed under Medication Comparison Studies.
Thioridazine Generic available Mellaril®	0 PubMed citations, June 2, 2010 Search terms: clinical trial [PT] AND thioridazine AND (child OR adolescent) NOT adult	None	No recent data.	None listed. However the following pediatric dosing guidelines are given: "For pediatric patients with schizophrenia who are unresponsive to other agents, the recommended initial dose is 0.5 mg/kg/day given in divided doses. Dosage may be increased gradually until optimum therapeutic effect is obtained or the maximum dose of 3 mg/kg/day has been reached." [1]	No clinical trials found in the last 10 years.

Table H

Typical Antipsychotics

First Generation Antipsychotics

Thiothixene Generic available Navane®	0 PubMed citations, June 2, 2010 Search terms: clinical trial [PT] AND thiothixene AND (child OR adolescent) NOT adult	None	No recent data.	No FDA approved pediatric marketing indications.	No clinical trials found in the last 10 years.
Fluphenazine Generic available Prolixin®	0 PubMed citations, June 2, 2010 Search terms: clinical trial [PT] AND fluphenazine AND (child OR adolescent) NOT adult	None	No recent data.	No FDA approved pediatric marketing indications.	No clinical trials found in the last 10 years.
Trifluoperazine Generic available Stelazine®	2 PubMed citations, June 2, 2010 Search terms: clinical trial [PT] AND trifluoperazine AND (child OR adolescent) NOT adult	None	No recent data.	No FDA approved pediatric marketing indications. However the following pediatric dosing guidelines are given in the FDA approved package insert: "Psychotic Children Dosage should be adjusted to the weight of the child and the severity of the symptoms. These dosages are for children ages 6 to 12, who are hospitalized or under close supervision." [1]	No clinical trials found in the last 10 years.

[1] Quotes are taken from individual medication webpages accessed from http://dailymed.nlm.nih.gov
[2] This quote only is taken from the FDA PDF accessed from link on
http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.Label_ApprovalHistory#apphist

Table I

Antipsychotics First and Second Generation (Typical and Atypical)

Antipsychotic Comparison Studies

Study & Funding source	Studies that met criteria	Safety	Efficacy	Conclusions Limitations Comments
Biederman J, Mick E, Hammerness P, Harpold T, Aleardi M, Dougherty M, Wozniak J. Open-label, 8-week trial of olanzapine and risperidone for the treatment of bipolar disorder in preschool-age children. Biol Psychiatry. 2005 Oct 1;58(7):589-94. PMID: 16239162 Funding Source: Stanley Medical Research institute RIS vs. OLZ	POL 8 wks 31 pts 4-6 yrs	Most common Adverse Events: Increased appetite Common cold symptoms (may not be related) Headache Sedation Weight gain: OLZ: 3.2 kg RIS: 2.2 kg Both > 7% body weight increase RIS associated with increase in prolactin levels. Other lab: no significant changes or differences between meds. Cardiac changes: OLZ: increased heart rate RIS: increased systolic pressure	Young Mania Rating Scale (YMRS) score: OLZ: -12.1 $p < 0.001$ RIS: -18.3 $p < 0.001$ Response: (criteria = Clinical Global Impression-Improvement score much/very much improved + YMRS change of ≥30) OLZ: 53% RIS: 69% $p = 0.4$ Difference not significant	"This prospective open study suggests that treatment with risperidone or olanzapine may result in a rapid reduction of symptoms of mania in preschool children with BPD." p. 589 "In addition, treatment with risperidone was also associated with a statistically significant improvement in symptoms of depression." p. 592 "In contrast, we did not find a robust response to symptoms of disruptive behavioral disorders (DBD) as has been documented for atypical antipsychotics in the literature..." p. 593 Limitations: short length, open label, no control group, use of spontaneous report of side effects, rating scales used not validated in this young population Comment: At time of study no appropriate validated rating scale instruments for this age group were readily available.
Migliardi G, Spina E, D'Arrigo C, Gagliano A, Germanò E, Siracusano R, Diaz FJ, de Leon J. Short- and long-term effects on prolactin of risperidone and olanzapine treatments in children and adolescents. Prog Neuropsychopharmacol Biol Psychiatry. 2009 Nov 13;33(8):1496-501. Epub 2009 Aug 23. PMID: 19706318 Funding Source: "No commercial organizations had any role in the writing of this paper for publication." RIS vs. OLZ	POL 12 mos 42 pts Mean age range 10.1 to 14.3 yrs Monotherapy with either RIS or OLZ Diagnosis independent study	Mean prolactin levels: RIS 4.9 ng/mL > than OLZ But after 12 mos differences were not significant. No symptoms of hyperprolactinemia except one case of transient mild galactorrhea that resolved without modification of dose.	Not studied.	"Our study showed a pattern consistent with the development of prolactin tolerance over time." p.1501 "...effects of all antipsychotics on prolactin are probably dose-related." p. 1501 Limitations: small, heterogeneous sample, lack of more frequent sampling for prolactin, compliance factors not ruled out Comment: Tolerance means that prolactin levels return to baseline over time in the continued presence of medication treatment. Symptomatic hyperprolactinemia is uncommon and transient in this study.

Table I

Antipsychotics First and Second Generation (Typical and Atypical)

Antipsychotic Comparison Studies

Study & Funding source	Studies that met criteria	Safety	Efficacy	Conclusions Limitations Comments
Sikich L, Frazier JA, McClellan J, Findling RL, Vitiello B, Ritz L, Ambler D, Puglia M, Maloney AE, Michael E, De Jong S, Slifka K, Noyes N, Hlastala S, Pierson L, McNamara NK, Delporto-Bedoya D, Anderson R, Hamer RM, Lieberman JA. Double-blind comparison of first- and second-generation antipsychotics in early-onset schizophrenia and schizo-affective disorder: findings from the treatment of early-onset schizophrenia spectrum disorders (TEOSS) study. Am J Psychiatry. 2008 Nov;165(11):1420-31. Epub 2008 Sep 15. Erratum in: Am J Psychiatry. 2008 Nov;165(11):1495. PMID: 18794207 Funding Source: NIMH; Pharmaceutical companies donated study medications RIS vs. OLZ vs. MOL	RCT 8 wks 116 pts 8-19 yrs SCZform disorders	Adverse Events Most pts experienced at least one AE. Frequent AE's: sedation, irritability, anxiety 8 pts hospitalized variously for: worsening psychosis 6, urinary retention 1, or suicidality 1): MOL: 2 OLZ: 2 RIS: 4 Discontinuation due to AE's: MOL: 8 pts OLZ: 6 pts RIS: 5 pts Adverse Events higher for certain meds: MOL: akathisia $p < 0.0008$ OLZ: wt gain $p < 0.001$ Increased appetite $p < 0.0019$ RIS: constipation $p < 0.021$ Wt gain: MOL: 0.3 kg not significant OLZ: 6.1 kg $p \leq 0.0001$ RIS: 3.6 kg $p \leq 0.0001$ EPS: MOL: 18% experienced moderate to severe akathisia Mild involuntary movements seen in 1 pt on each med. Prolactin: Elevated in RIS group QT interval increased significantly in OLZ group	Clinical Global Impression-Improvement (CGI-I) improved: MOL: 60% OLZ: 49% RIS: 46% Positive & Negative Symptom Scale (PANSS) score change: MOL: -27.0 $p < 0.0001$ OLZ: -26.6 $p < 0.0001$ RIS: -23.7 $p < 0.0001$ No significant difference in response rates (CGI-I much or very much improved & PANSS score ≥20% reduction): MOL: 50% OLZ: 34% RIS: 46%	"Olanzapine and risperidone were associated with significantly greater weight gain. Olanzapine showed the greatest risk of weight gain and significant increases in fasting cholesterol, low density lipoprotein, insulin, and liver transaminase levels. Molindone led to more self-reports of akathisia." p. 1420 "Risperidone and olanzapine did not demonstrate superior efficacy over molindone for treating early-onset schizophrenia and schizoaffective disorder. Adverse effects were frequent but differed among medications. The results question the nearly exclusive use of second-generation antipsychotics to treat [this population]..." p. 1420 Limitations: no placebo control, sample size, length of study insufficient to detect tardive dyskinesia, use of prophylactic benztropine for those receiving molindone, uncommon use of molindone in clinical practice compared to other first generation meds, failure to be able to include newer second generation antipsychotics. Comments: True incidence of EPS in those receiving molindone can not be gauged due to use of benztropine in this group. As the major difference between first and second generation antipsychotics (based upon this study) appears to be their side effect profiles, this issue limits the ability to compare the medication side effect profiles in this area. **Molindone has been discontinued by the manufacturer.**
Castro-Fornieles J, Parellada M, Soutullo CA, Baeza I, Gonzalez-Pinto A, Graell M, Paya B, Moreno D, de la Serna E, Arango C. Antipsychotic treatment in child and adolescent first-episode psychosis: a longitudinal naturalistic approach. J Child Adolesc Psychopharmacol. 2008 Aug;18(4):327-36. PMID: 18759642 Funding Source: Carlos III Institute of Health, Spanish Department of Health, Cooperative Research Thematic Network; Spanish Ministry of Health, CIBERSAM Network. RIS vs. QTP vs. OLZ	POL 6 mos 110 pts 9-17 yrs Psychosis	Adeverse Events: Weight, gain: OLZ: 11.7 kg QTP: 6.0 kg RIS: 1.9 kg OLZ > RIS $p = 0.020$ OLZ > QTP $p = 0.040$ UKU total scores: OLZ: 7.3 QTP: 7.9 RIS: 9.6 RIS > OLZ for neurological AE's $p = 0.022$ UKU = Udvalg for Kliniske Undersogelser Side Effects Rating Scale	Positive & Negative Symptom Scale score change: OLZ: -36.5 $p < 0.001$ QTP: -32.8 $p < 0.001$ RIS: -25.4 $p < 0.001$ Clinical Global Impression score change: OLZ: -1.7 $p < 0.001$ QTP: -2.8 $p < 0.001$ RIS: -2.3 $p < 0.001$	"... no significant differences were found in the reductions on any scale in patients treated with risperidone, quetiapine, or olanzapine for 6 months." p. 327 "These three obtain similar clinical improvement but differ in their side effects." p. 327 Limitations: no randomization, open label, heterogeneity in groups, sample size, no objective analysis of compliance

Table I

Antipsychotics First and Second Generation (Typical and Atypical)

Antipsychotic Comparison Studies

Study & Funding source	Studies that met criteria	Safety	Efficacy	Conclusions Limitations Comments
Jensen JB, Kumra S, Leitten W, Oberstar J, Anjum A, White T, Wozniak J, Lee SS, Schulz SC. A comparative pilot study of second-generation antipsychotics in children and adolescents with schizophrenia-spectrum disorders. J Child Adolesc Psychopharmacol. 2008 Aug;18(4):317-26. PMID: 18759641 Funding Source: Astra-Zeneca (JJ). RIS vs. OLZ vs. QTP	POL 12 wks 30 pts 10-18 yrs SCZ spectrum disorder	Most common Adverse Events: Muscle stiffness/akathisia Sedation Increased agitation Increased appetite 1 pt on RIS developed mastitis without galactorrhea ≥7% wt. gain: all meds: 63% Weight gain on RIS & OLZ roughly equal and greater than on QTP. No clinically significant changes in lab, vital signs, or EKG's with any med.	# of responders as measured by Positive & Negative Symptom Scale (PANSS) score reduction ≥40%: OLZ: 5 of 10 QTP: 3 of 10 RIS: 7 of 10	"A greater proportion of adolescents (7 of 10) treated with risperidone met responder criteria (i.e., ≥40% reduction in PANSS total and subscale scores) as compared to adolescents treated with quetiapine or adolescents (5 of 10) treated with olanzapine. However this difference did not reach significance..." Limitations: open label, small sample size, short length Comments: This study was not meant to show definitive results in comparative treatment response. It was designed to help plan a future RCT.
Mozes T, Ebert T, Michal SE, Spivak B, Weizman A. An open-label randomized comparison of olanzapine versus risperidone in the treatment of childhood-onset schizophrenia. J Child Adolesc Psychopharmacol. 2006 Aug;16(4):393-403. PMID: 16958565 Funding Source: None stated. OLZ vs. RIS	POL 12 wks 25 pts 9-14 yrs Childhood onset Schizophrenia	Dropout Rate: OLZ: 8.3% RIS: 30.8% p = 0.161 Not significant. OLZ: 1 dropout was due lost to followup RIS: 3 dropped out due to lack of improvement and 1 due to severe hyperprolactinemia and growth hormone reduction Extrapyramidal symptoms: No significant difference between meds Weight gain: OLZ: 5.78 kg RIS: 2.87 kg p = 0.33 No significant difference between meds.	% change Positive & Negative Symptom Scale scores: OLZ: -40.78% p < 0.001 RIS: -47.99% p < 0.001 Difference not significant	"Both olanzapine and risperidone are efficacious and relatively safe in the treatment of COS [childhood onset schizophrenia], with a slight statistically nonsignificant advantage of olanzapine in the dimensions of negative symptoms and dropout rate." p. 402 Limitations: open label, small sample size, short length, co-treatment by other meds, lack of placebo control
Shaw P, Sporn A, Gogtay N, Overman GP, Greenstein D, Gochman P, Tossell JW, Lenane M, Rapoport JL. Childhood-onset schizophrenia: A double-blind, randomized clozapine-olanzapine comparison. Arch Gen Psychiatry. 2006 Jul;63(7):721-30. PMID: 16818861 Funding Source: None stated, but presumably NIMH & NIH as all authors work at one or the other agency. CZP vs OLZ	RCT 8 wks (+ 2 yr POL) 25 pts 7-16 yrs Childhood onset SCZ	CZP associated with more hypertension, tachycardia, and enuresis Weight gain: CZP: +3.6 kg OLZ: +3.6 kg Extrapyramidal symptoms: few symptoms and no treatment differences in overall change EKG changes: CZP: 2 pts OLZ: 1 pts None required med change WBC changes: CZP: 2 pts with transient drop OLZ: 1 pt with transient drop No significant changes in liver function tests.	Compared to baseline without antipsychotic treatment: Clinical Global Impression-Severity change Effect Size: CZP: 1.4 OLZ: 0.5 Scale for Assessment of Negative Symptoms change Effect size CZP: 1.6 OLZ: 1.3 Scale for Assessment of Positive Symptoms change Effect size: CZP: 1.0 OLZ: 1.0	"While not demonstrating definitively the superiority of clozapine compared with olanzapine in treatment-refractory childhood-onset schizohprenia, the study suggests that clozapine has a more favorable profile of clinical response, which is balanced against more associated adverse events." p 721 Limitations: no placebo control, differences in dose escalation between groups, short length, small sample, inpatient setting

Table I

Antipsychotics First and Second Generation (Typical and Atypical)

Antipsychotic Comparison Studies

Study & Funding source	Studies that met criteria	Safety	Efficacy	Conclusions Limitations Comments
Staller J. The effect of long-term antipsychotic treatment on prolactin. J Child Adolesc Psychopharmacol. 2006 Jun;16(3):317-26. PMID: 16768639 Funding Source: Astra-Zeneca Pharmaceuticals in part OLZ vs. QTP vs. RIS	ROL* *Retrospective Open Label ≥6 mos* 50 pts 5-17 yrs Treatment with OLZ, QTP, or RIS Diagnosis Independent Study	Mean prolactin level: Control: 6.4 ng/mL $p < 0.001$ OLZ: 10.4 ng/mL $p < 0.001$ QTP: 6.7 ng/mL $p < 0.001$ RIS: 22.0 ng/mL $p < 0.001$ 12% overall reported changes in sexual functioning or *menstrual/breast problems	Effectiveness not part of study	"The risk of hyperprolactinemia with long-term use of risperidone appears to be significantly greater than for olanzapine or quetiapine." p. 317 Limitations: retrospective, open label, small sample size especially for olanzapine, other non-antipsychotic med use permitted, brief sampling period, does not address other antipsychotics Comment: All elevations of prolactin were mild.
Sikich L, Hamer RM, Bashford RA, Sheitman BB, Lieberman JA. A pilot study of risperidone, olanzapine, and haloperidol in psychotic youth: a double-blind, randomized, 8-week trial. Neuropsychopharmacology. 2004 Jan;29(1):133-45. PMID: 14583740 Funding Source: NIMH; NIH; Janssen Pharmaceutica; Eli Lilly Company; Foundation of Hope. In Jensen RIS vs. OLZ vs. HAL	RCT 8 wks 50 pts 8-19 yrs Psychosis	Common adverse effects; Mild to mod sedation Extrapyramidal symptoms (EPS) Weight gain Weight gain/BMI HAL: +3.6 kg/+1.2 $p = 0.0009/0.0015$ OLZ: +7.2 kg/+2.4 $p = 0.0002/0.0001$ RIS: 4.9 kg/+1.6 $p = 0.0001/0.0001$ Differences between meds not statistically significant. Cardiac: Qtc increase for HAL Lab: Liver Function Test increases in 2 pts on RIS Glucose increases for OLZ Mild prolactin increases for HAL and RIS EPS: >50% in all groups had mild EPS some requiring anticholinergics to treat; HAL greater than other meds 2 pts on HAL withdrew due to severe dystonia	BPRS-C total score reduction: HAL: -11 $p = 0.0018$ OLZ: -28 $p = 0.0018$ RIS: -27 $p = 0.0018$ Responders (CGI of much or very much improved and ≥20% reduction in BPRS-C: HAL: 53% OLZ: 88% RIS: 74% Between group differences not significant.	"....this study provides initial controlled data that risperidone and olanzapine are effective in reducing psychotic symptoms in children and adolescents with a variety of diagnoses. These two atypical agents have lower risk for acute, severe EPS than the traditional agent haloperidol. However, EPS is identified at much higher rates than observed in comparable adult populations. Weight gain is found in all treatment groups and remains an important concern." p144 Limitations: small sample size, diagnostic heterogeneity, other med use permitted, variations in age and pubertal status
Kumra S, Kranzler H, Gerbino-Rosen G, Kester HM, De Thomas C, Kafantaris V, Correll CU, Kane JM. Clozapine and "high-dose" olanzapine in refractory early-onset schizophrenia: a 12-week randomized and double-blind comparison. Biol Psychiatry. 2008 Mar 1;63(5):524-9. Epub 2007 Jul 25. PMID: 17651705 Funding Source: NIMH CZP vs. OLZ	RCT 12 wk 39 pts 10-18 yrs Schizophrenia or schizoaffective disorder	3 pts withdrew from study due to Adverse Effects: Neutropenia (1) and Weight gain (2) 2 other pts experienced significant AE's Bowel obstruction Drug inducted diabetes >7% wt gain: 13% (of all study pts) Trigylceride abnormality 23% (of all study pts)	Brief Psychiatric Rating Scale (BPRS) scores changes: CZP: -21.9 OLZ: -14.6 ES: 0.29 Low effect size. Clinical Global Impression-Improvement (CGI-I) score: CZP: 2.03 OLZ: 3.1 ES: 0.59 Moderate effect size. Responded (decrease ≥ 30% on BPRS and CGI-I of much/very much improved): CZP: 66% OLZ: 33%	"This double-blind randomized comparison of two second-generation antipsychotic drugs for treatment-refractory adolescents with schizophrenia supports clozapine as the agent of choice." p. 524 "With the exception of negative symptoms, all treatment condition x time interactions for outcome measure were not statistically significant." p.527 Limitations: small sample size, other med use permitted, subjects included who although randomized did not take study med at high dose Comment: Only difference between meds appears to be effect on negative symptoms, which comes with increased risk of adverse effects.

Table I

Antipsychotics First and Second Generation (Typical and Atypical)

Antipsychotic Comparison Studies

Study & Funding source	Studies that met criteria	Safety	Efficacy	Conclusions Limitations Comments
Fraguas D, Merchán-Naranjo J, Laita P, Parellada M, Moreno D, Ruiz-Sancho A, Cifuentes A, Giráldez M, Arango C. Metabolic and hormonal side effects in children and adolescents treated with second-generation antipsychotics. J Clin Psychiatry. 2008 Jul;69(7):1166-75. PMID: 18588363 Funding Source: Spanish Ministry of Health, Instituto de Salud Carlos III; Miguel Angel Martin Investigation Grant; NARSAD 2005: Independent Investigator Award. OLZ vs. QTP vs. RIS	POL 6 mos 66 pts mean age: 15.2 yrs Treatment with OLZ, QTP, or RIS Diagnosis Independent Study	Weight gain/BMI OLZ: +3.7 kg/+3.7 QTP: +2.7 kg/+2.7 RIS: +1.4 kg/+1.4 At risk for adverse outcome (≥85th BMI percentile AND presence of 1 or more abnormal lab or hypertension; or ≥95th BMI percentile) Baseline: 11 pts End: 25 pts Only variable related to being at risk at end of treatment was being at risk at beginning of treatment.	Effectiveness not part of study	"Our results showed that after only 6 months of follow-up, BMI z scores [age/gender corrected] increased significantly in patients receiving olanzapine and risperidone, and total cholesterol levels increased significantly in patients cereiving olanzapine and quetiapine. Indeed, treatment with olanzapine was associated with both weight gain....and increased risk of adverse health outcome." p. 1172 Limitations: small sample size, no randomization, open label, heterogeneity of diagnosis & past history, heterogeneity of dosages, differential drop out rate, beginning age/gender adjusted BMI different between groups, other non-antipsychotic med use permitted Comment: It would appear that patients already overweight at the beginning of treatment are at the highest risk of experiencing more weight gain and adverse health outcomes.
Kumra S, Kranzler H, Gerbino-Rosen G, Kester HM, DeThomas C, Cullen K, Regan J, Kane JM. Clozapine versus "high-dose" olanzapine in refractory early-onset schizophrenia: an open-label extension study. J Child Adolesc Psychopharmacol. 2008 Aug;18(4):307-16. PMID: 18759640 Funding Source: NIMH CZP vs. OLZ	POL 12 wks 33 pts 10-18 yrs Schizophrenia or Schizoaffective disorder	After previous RCT [CLZ2], numbers of pts that switched med for open label study: CZP: 2 due to unacceptable side effects) OLZ: 10 due to inadequate response 1 due to unacceptable side effects 1 due to desire to increase response on CZP 32% of pts >7% weight gain 20% had elevated cholesterol 56% had elevated triglycerides 15% had elevated glucose 36% had elevated prolactin	After previous RCT [CLZ2] % that stayed on original med for open label study: CZP: 86% OLZ: 42%	"Adolescents with a poor response to olanzapine may do better on clozapine." p. 307 "...clozapine continued to have an apparent advantage in treatment-resistant patients..." p. 314 "...both clozapine and olanzapine were particularly problematic, and perhaps more so in youth as compared to adults, with regard to metabolic side effects." p. 314 Limitations: small sample size, open label, other med use permitted Comment: This study addresses treatment resistant pts and may not be generalizable to any other populations.
Bastiaens L. A non-randomized, open study with aripiprazole and ziprasidone for the treatment of aggressive behavior in youth in a community clinic. Community Ment Health J. 2009 Feb;45(1):73-7. Epub 2008 Jul 3. PMID: 18597173 Funding Source: Not stated. ARI vs. ZPS	POL 2 mos 46 pts 6-18 yrs Aggression (Multiple diagnoses	Most common Adverse Effects: Sedation 50% Extrapyramidal symptoms 10% Dizziness 10% Nausea 10% Headache 10% Weight gain 10% 4 pts lost to followup 8 withdrew due to excessive sedation Overall 71% of completers experienced side effects.	Overt Aggression Scale (OAS) change: ARI: -4.5 p = 0.0005 ZPS: -4.3 p = 0e0018 Overall % showing OAS improvement: 63% Clinical Global Impression-Improvement 2.1 No significant difference on any measure between ARI and ZPS	"In this naturalistic treatment setting, the use of aripiprazole or ziprasidone was highly effective in targeting aggressive behavior in children and adolescents with a variety of diagnoses." Limitations: diagnostic heterogeneity, no randomization, short length, no analysis of adherence, no data on drop-outs Comment: In adults ARI and ZPS generally elicit the fewest side effects. Unclear if the tendency for SGAs to elicit more side effects in kids washes out this potential benefit of the use of these particular SGAs.

Table I

Antipsychotics First and Second Generation (Typical and Atypical)

Antipsychotic Comparison Studies

Study & Funding source	Studies that met criteria	Safety	Efficacy	Conclusions Limitations Comments
Swadi HS, Craig BJ, Pirwani NZ, Black VC, Buchan JC, Bobier CM. A trial of quetiapine compared with risperidone in the treatment of first onset psychosis among 15- to 18-year-old adolescents. Int Clin Psychopharmacol. 2010 Jan;25(1):1-6. PMID: 19809337 Funding Source: AstraZeneca. QTP vs. RIS	POL (Single blind) 6 wks 22 pts < 19 yrs First Onset Psychosis	Adverse Events (AE) AE / QTP / RIS / p AIMs 9.1% 27.3% 0.586 Prolactin 9.1% 90.9% 0.001 >10% wt 27.3% 9.1% 0.586 AIMS = Abnormal Involuntary Movement Scale BARS = Barnes Akathisia Scale Quetiapine causes more weight gain. Risperidone causes more extrapyramidal symptoms.	% that responded (≥30% reduction in measure) at 6 wks: Mea / QTP / RIS / p PANSS 54.5 72.7 0.659 BPRS 54.5 45.5 1.0 HAM-D 50.0 70.0 0.65 YMRS 63.6 90.0 0.311 PANSS = Positive & Negative Symptom Scale BRPS = Brief Psychiatric Rating Scale HAM-D = Hamilton Depression Rating Scale YMRS = Young Mania Rating Scale	"In this small adolescent treatment study, a number of statistically nonsignificant, but clinically notable differences seem to favour the efficacy of risperidone over quetiapine." p.5 Limitations. small sample size, short length, capped maximal dose Comment: Study conclusion favored risperidone over quetiapine although maker of quetiapine funded study, but statistically not significant.
Miral S, Gencer O, Inal-Emiroglu FN, Baykara B, Baykara A, Dirik E. Risperidone versus haloperidol in children and adolescents with AD : a randomized, controlled, double-blind trial. Eur Child Adolesc Psychiatry. 2008 Feb;17(1):1-8. Epub 2007 Dec 13. PMID: 18080171 Funding Source: In part by Janssen and Cilag Drug Company RIS vs. HAL	RCT 12 wks 30 pts 8-18 yrs Autism	Prolactin increase with RIS. ALT (Liver function enzyme): Increased in HAL Decreased in RIS Weight gain: RIS: +4.3 kg HAL: +4.6 kg Difference between RIS and HAL not statistically significant Extrapyramidal symptoms: Change in ESRS score for HAL significant for worsening. ESRS = Chouinard Extrapyramidal Symptoms Rating Scale	RIS superior to HAL on Scale / p RLRS Sensory-motor 0.0977 RLRS Language 0.0799 ABC 0.0063 Turgay DSM-IV PDD 0.0052 RLRS = Ritvo-Freeman Real Life Rating Scale ABC = Aberrant Behavior Checklist PDD = Pervasive Developmental Disorder	"Risperidone was found to be more effective than haloperidol in the treatment of behavioral symptoms, impulsivity, language skills, and impaired social relations in children with AD [autism disorder]. The results demonstrated that both drugs were safe and well tolerated in the treatment of AD." p. 1 Limitations: small sample size, heterogeneous sample
Gencer O, Emiroglu FN, Miral S, Baykara B, Baykara A, Dirik E. Comparison of long-term efficacy and safety of risperidone and haloperidol in children and adolescents with autistic disorder. An open label maintenance study. Eur Child Adolesc Psychiatry. 2008 Jun;17(4):217-25. PMID: 18026891 Funding Source: In part by Janssen and Cilag Drug Company. RIS vs. HAL	POL 24 wks 28 pts 8-18 yrs Autism	Prolactin increase with HAL but difference between RIS and HAL not significant. Weight gain: RIS: +4.2 kg HAL: +6.3 kg Difference between RIS and HAL not statistically significant Extrapyramidal symptoms: minimal and difference between RIS and HAL not statistically significant	At endpoint RIS superior to HAL on: Scale / p CGI-I 0.0186 RSRL Language 0.014 ABC 0.0063 Turgay DSM-IV PDD 0.0594 RLRS = Ritvo-Freeman Real Life Rating Scale ABC = Aberrant Behavior Checklist PDD = Pervasive Developmental Disorder On other measures (ABC, other RF subscales) RIS vs HAL showed no significant difference	"This study reveals that in the long-term maintenance treatment of AD [autism disorder], risperidone is more effective and well tolerated than haloperidol, the most frequent studied and effective psychopharmacological agent of previous years." p. 224 Limitations: open label, small sample size, no analysis of intelligence level and response Comments: Several improvements noted with RIS by a previous RCT on the same sample are not borne out long- term in this open label continuation study. See study above [RIS21]. Difference in EPS between RIS and HAL not significant in this study and minimal for both conditions.

Table I

Antipsychotics First and Second Generation (Typical and Atypical)

Antipsychotic Comparison Studies

Study & Funding source	Studies that met criteria	Safety	Efficacy	Conclusions Limitations Comments
Gilbert DL, Batterson JR, Sethuraman G, Sallee FR. Tic reduction with risperidone versus pimozide in a randomized, double-blind, crossover trial. J Am Acad Child Adolesc Psychiatry. 2004 Feb;43(2):206-14. PMID: 14726728 Funding Source: TEVA Pharmaceuticals; National Institute of Neurological Disorders and Stroke. RIS vs. PIM	RCT 4 wks + 2 wk washout + 4 wks 19 pts 7-17 yrs Tourette's or Chronic Motor Tic Disorder	ECG: no changes either med Wt. gain RIS: 1.9 kg PIM: 1.0 kg No serious Adverse Effects. 6 of 19 (32%) failed to complete study, but none due to adverse effects.	Yale Global Tic Severity Scale change: RIS: -18.1 PIM: -9.1 p = 0.05	"In this study, risperidone appeared superior to pimozide for tic suppression but was associated with greater weight gain. Limitations: small sample size, suboptimal compliance rate, comorbid disorders present, statistical limitations of crossover design, no pcontrol group, most severely afflicted pts not part of study
Gothelf D, Apter A, Reidman J, Brand-Gothelf A, Bloch Y, Gal G, Kikinzon L, Tyano S, Weizman R, Ratzoni G. Olanzapine, risperidone and haloperidol in the treatment of adolescent patients with schizophrenia. J Neural Transm. 2003 May;110(5):545-60. PMID: 12721815 Funding Source: Hilda and Philippe Setton supported research program on behavioral genetics and schizophrenia. OLZ vs RIS vs HAL	POL 8 wks 43 Average age ~17 SCZ	No patients discontinued the study due to Adverse Effects Common Adverse Effects: Fatigability: RIS: 11.8% OLZ: 42.1 % HAL: 71.4% Increased depression: RIS: 11.8% OLZ: 26.3% HAL: 71.4% p < 0.01 Cognitive side effects: more common with OLZ and HAL than RIS Any extrapyramidal symptom: RIS: 23.6% OLZ: 11.8% HAL: 57.2Y Weight gain not reported (in a different article by same research group).	Positive & Negative Symptom Scale Total Score Changes: RIS: -16.3 OLZ: -10.6 HAL: -19.8 No p values reported for individual meds or for differences between meds.	"Olanzapine, risperidone and haloperidol appear to be equally effective for the treatment of schizophrenia in adolescent inpatients but have different side effect profiles." p. 545 "Olanzapine and haloperidol induce fatigability more frequently than risperidone. Haloperidol was associated with a higher frequency of depression and more severe extrapyramidal symptoms." p. 545 Limitations: small sample size, short length, no randomization, open label, non-specialized rating scales used, smaller number of pts on haloperidol Comment: Note that cognitive side effects more common with HAL and OLZ.

APPENDIX A

Note on Appendix A

At the time the H.B. 2163 report was shared with stakeholders for comment, Appendix A contained the September 2010 draft of the *Psychotropic Medication Utilization Parameters for Foster Children*. Since then, the 2010 version of the Texas Parameters has been finalized and released by the Department of Family and Protective Services.

In order to provide the most current information with this report, in Appendix A HHSC replaced the September 2010 draft parameters with the recently released December 2010 parameters. A cover letter from the DFPS commissioner and the December 2010 parameters follow.

APPENDIX A

TEXAS DEPARTMENT OF FAMILY AND PROTECTIVE SERVICES

COMMISSIONER
Anne Heiligenstein

December 1, 2010

Dear Foster Care Network:

It is my pleasure to present to you the updated *Psychotropic Medication Parameters for Foster Children*. This update has been developed by the Texas Department of Family and Protective Services (DFPS) and the University of Texas at Austin College of Pharmacy along with a work group of experts with input from the Federation of Texas Psychiatry, Texas Pediatric Society, Texas Academy of Family Physicians and Texas Medical Association.

Children in foster care often have profound medical, psychological and social needs. Health care professionals, foster parents, and caregivers accept the challenge of meeting these needs each day. For some children, psychotropic medications can offer relief from some of the trauma of abuse and neglect and provide an opportunity for longer term improvement and a more meaningful and productive future. But the over reliance on psychotropic drugs to treat foster children has drawn criticism.

DFPS, along with the Department of State Health Services and the Health and Human Services Commission, responded to these complaints and in 2005 developed the *Psychotropic Medication Utilization Parameters for Foster Children*. The *Parameters* were updated in 2007 and again with this publication. The goal then, as it is now, was to support the safe, effective, and appropriate administration of these psychotropic medications. The *Parameters* offer health care providers, staff, and caregivers valuable information to consider when these medications are being prescribed to foster children.

The implementation of the *Parameters* has resulted in a significant decrease in utilization of psychotropic medications among foster children in Texas, and the guidelines have been influential in the development of several other states' monitoring efforts. In addition to the Parameters, in April 2008, STAR Health was implemented to manage the medical and behavioral health services for Texas foster children. STAR Health provides direct child psychiatric consultation to prescribing physicians leading to further improvements in the prescribing regimens for the children. STAR Health also utilizes an electronic health record (the Health Passport) for foster children that provides real-time availability of prescription and encounter data, which in turn results in a more carefully monitored delivery of care for the children.

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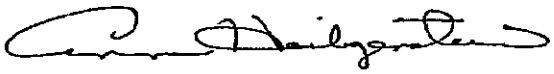
These updated *Parameters* include an expanded narrative section, updated references, medications introduced since the last update as well as more detailed information regarding indications for usage, warnings and precautions, age specific dosage ranges and metabolic monitoring where indicated.

We seek to build on these improvements and further improve the care of Texas foster children as we continue to protect the unprotected.

Sincerely,



Anne Heiligenstein

APPENDIX A

Psychotropic Medication Utilization Parameters for Foster Children

Developed by:
Texas Department of Family and Protective Services
and
The University of Texas at Austin College of Pharmacy

with review and input provided by:

- *Federation of Texas Psychiatry*
- *Texas Pediatric Society*
- *Texas Academy of Family Physicians*
- *Texas Medical Association*

December 2010

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Psychotropic Medication Utilization Parameters for Foster Children

Introduction and General Principles

The use of psychotropic medications by children is an issue confronting parents, other caregivers, and health care professionals across the United States. Foster children, in particular, have multiple needs, including those related to emotional or psychological stress. Foster children typically have experienced abusive, neglectful, serial or chaotic care taking environments. Birth family history is often not available. These children often present with a fluidity of different symptoms over time reflective of past traumatic and reactive attachment difficulties that may mimic many overlapping psychiatric disorders. Establishment of rapport is often difficult. These multiple factors serve to complicate diagnosis. Foster children may reside in areas of the state where mental health professionals such as child psychiatrists are not readily available. Similarly, caregivers and health providers may be faced with critical situations that require immediate decisions about the care to be delivered. For these and other reasons, a need exists for treatment guidelines and parameters regarding the appropriate use of psychotropic medications in foster children.

Because of the complex issues involved in the lives of foster children, it is important that a comprehensive evaluation be performed before beginning treatment for a mental or behavioral disorder. Except in the case of an emergency, a child should receive a thorough health history, psychosocial assessment, mental status exam, and physical exam before the prescribing of psychotropic medication. Psychological testing may be particularly useful in clarifying a diagnosis and informing appropriate treatment. The physical assessment should be performed by a physician or another healthcare professional qualified to perform such an assessment. It is recognized that in some situations, it may be in the best interest of the child to prescribe psychotropic medications before a physical exam can actually be performed. In these situations, a thorough health history should be performed to assess for significant medical disorders and past response to medications, and a physical evaluation should be performed as soon as possible. The mental health assessment should be performed by an appropriately qualified mental health professional or appropriate primary care physician with experience in providing mental health care to children. The child's symptoms and functioning should be assessed across multiple domains, and the assessment should be developmentally appropriate. It is very important that information about the child's history and current functioning be made available to the treating physician in a timely manner, either through an adult who is well-informed about the child or through a comprehensive medical record. It is critical to meet the individual needs of patients and their families in a culturally competent manner. This indicates a need to address communication issues as well as differences in perspective on issues such as behavior and mental functioning. At present there are no biomarkers to assist with the diagnosis of mental disorders, and imaging (e.g., MRI) and other tests (e.g., EEG) are not generally helpful in making a clinical diagnosis of a mental disorder.

The role of non-pharmacological interventions should be considered before beginning a psychotropic medication, except in urgent situations such as suicidal ideation, psychosis, self injurious behavior, physical aggression that is acutely dangerous to others, or severe impulsivity endangering the child or others; when there is marked disturbance of psychophysiological functioning (such as profound sleep disturbance), or when the child shows marked anxiety, isolation, or withdrawal. Given the unusual stress and change in environmental circumstances associated with being a foster child, counseling or psychotherapy should generally begin before or concurrent with prescription of a psychotropic medication. Patient and caregiver education about the mental disorder, treatment options (non-pharmacological and pharmacological), treatment expectations, and potential side effects should occur before and during the prescription of psychotropic medications.

It is recognized that many psychotropic medications do not have Food and Drug Administration (FDA) approved labeling for use in children. The FDA has a statutory mandate to determine whether pharmaceutical company sponsored research indicates that a medication is safe and effective for those indications that are listed in the approved product labeling. The FDA assures that information in the approved product labeling is accurate, and limits the manufacturer's marketing to the information contained in the approved labeling. ***The FDA does not regulate physician and other health provider practice. In fact, the FDA has stated that it does "not limit the manner in which a practitioner may prescribe an approved drug." Studies and expert clinical experience often support the use of a medication for an "off-label" use.*** Physicians should utilize the available evidence, expert opinion, their own clinical experience, and exercise their clinical judgment in prescribing what is best for each individual patient.

Role of Primary Care Providers

Primary care providers play a valuable role in the care of youth with mental disorders. Not only are they the clinicians most likely to interact with children who are in distress due to an emotional or psychiatric disorder, inadequate numbers of child psychiatrists are available to meet all of the mental health needs of children. Primary care clinicians are in an excellent position to perform screenings of children for potential mental disorders, and they should be able to diagnose and treat relatively straightforward situations such as uncomplicated ADHD, anxiety, or depression. As always, consideration should be given regarding the need for referral for counseling, psychotherapy, or behavioral therapy.

Primary care providers vary in their training, clinical experience, and confidence to address mental disorders in children. Short courses and intensive skills oriented seminars may be beneficial in assisting primary clinicians in caring for children with mental disorders. Active liaisons with child psychiatrists who are available for phone consultation or referral can be beneficial in assisting primary care clinicians to meet the mental health needs of children.

General principles regarding the use of psychotropic medications in children include:

- A DSM-IV (or current edition) psychiatric diagnosis should be made before the prescribing of psychotropic medications.
- Clearly defined target symptoms and treatment goals for the use of psychotropic medications should be identified and documented in the medical record at the time of or before beginning treatment with a psychotropic medication. These target symptoms and treatment goals should be assessed at each clinic visit with the child and caregiver. Whenever possible, recognized clinical rating scales (clinician, patient, or caregiver assessed, as appropriate) or other measures should be used to quantify the response of the child's target symptoms to treatment and the progress made toward treatment goals.
- In making a decision regarding whether to prescribe a psychotropic medication in a specific child, the clinician should carefully consider potential side effects, including those that are uncommon but potentially severe, and evaluate the overall benefit to risk ratio of pharmacotherapy.
- Except in the case of an emergency, informed consent should be obtained from the appropriate party(s) before beginning psychotropic medication. Informed consent to treatment with psychotropic medication entails diagnosis, expected benefits and risks of treatment, including common side effects, discussion of laboratory findings, and uncommon but potentially severe adverse events. Alternative treatments, the risks associated with no treatment, and the overall potential benefit to risk ratio of treatment should be discussed.
- During the prescription of psychotropic medication, the presence or absence of medication side effects should be documented in the child's medical record at each visit.
- Appropriate monitoring of indices such as height, weight, blood pressure, or other laboratory findings should be documented.
- Monotherapy regimens for a given disorder or specific target symptoms should usually be tried before polypharmacy regimens.
- Doses should usually be started low and titrated carefully as needed.
- Only one medication should be changed at a time, unless a clinically appropriate reason to do otherwise is documented in the medical record. (Note: starting a new medication and beginning the dose taper of a current medication is considered one medication change).
- The use of "prn" or as needed prescriptions is discouraged. If they are used, the situation indicating need for the administration of a prn medication should be clearly indicated as well as the maximum number of prn doses in a day and a week. The frequency of administration should be monitored to assure that these do not become regularly scheduled medications.
- The frequency of clinician follow-up with the patient should be appropriate for the severity of the child's condition and adequate to monitor response to treatment, including: symptoms, behavior, function, and potential medication side effects.
- In depressed children and adolescents, the potential for emergent suicidality should be carefully evaluated and monitored.
- If the prescribing clinician is not a child psychiatrist, referral to or consultation with a child psychiatrist, or a general psychiatrist with significant experience in treating children, should occur if the child's clinical status has not experienced meaningful improvement within a timeframe that is appropriate for the child's clinical response and the medication regimen being used.
- Before adding additional psychotropic medications to a regimen, the child should be assessed for adequate medication adherence, accuracy of the diagnosis, the occurrence of comorbid disorders (including substance abuse and general medical disorders), and the influence of psychosocial stressors.
- If a medication is being used in a child for a primary target symptom of aggression associated with a DSM-IV nonpsychotic diagnosis (e.g., conduct disorder, oppositional defiant disorder, intermittent explosive disorder), and the behavior disturbance has been in remission for six months, then serious consideration should be given to slow tapering and discontinuation of the medication. If the medication is continued in this situation, the necessity for continued treatment should be evaluated at a minimum of every six months.
- The clinician should clearly document care provided in the child's medical record, including history, mental status assessment, physical findings (when relevant), impressions, adequate laboratory monitoring specific to the drug(s) prescribed at intervals required specific to the prescribed drug and potential known risks, medication response, presence or absence of side effects, treatment plan, and intended use of prescribed medications.

Use of Psychotropic Medication in Preschool Age Children

The use of psychotropic medication in young children of preschool ages is a practice that is limited by the lack of evidence available for use of these agents in this age group. The Preschool Psychopharmacology Working Group (PPWG) published guidelines summarizing available evidence for use of psychotropic medications in this age group (Gleason 2007). The PPWG was established in response to the clinical needs of preschoolers being treated with psychopharmacological agents and the absence of systematic practice guidelines for this age group, with its central purpose to attempt to promote an evidence-based, informed, and clinically sound approach when considering medications in preschool-aged children.

The PPWG guidelines emphasize consideration of multiple different factors when deciding on whether to prescribe psychotropic medications to preschool-aged children. Such factors include the assessment and diagnostic methods utilized in evaluating the child for psychiatric symptoms/illness, the current state of knowledge regarding the impact of psychotropic medication use on childhood neurodevelopmental processes, the regulatory and ethical contexts of use of psychotropic medications in small children (including available safety information and FDA status), and the existing evidence base for use of psychotropic medication in preschool aged children.

The publication includes specific guidelines and algorithm schematics developed by the PPWG to help guide treatment decisions for a number of psychiatric disorders that may present in preschool-aged children, including Attention-Deficit Hyperactivity Disorder, Disruptive Behavioral Disorders, Major Depressive Disorder, Bipolar Disorder, Anxiety Disorders, Post-Traumatic Stress Disorder, Obsessive-Compulsive Disorder, Pervasive Developmental Disorders, and Primary Sleep Disorders.

The working group's key points and guidelines are similar to the general principles regarding the use of psychotropic medication in children already detailed in this paper. However, the working group's algorithms put more emphasis on treating preschool-aged children with nonpsychopharmacological interventions (for up to 12 weeks) before starting psychopharmacological treatment, in an effort to be very cautious in introducing psychopharmacological interventions to rapidly developing preschoolers. The working group also emphasizes the need to assess parent functioning and mental health needs, in addition to training parents in evidence-based behavior management, since parent behavior and functioning can have a large impact on behavior and symptoms in preschool-aged children.

Therapeutic Controversies

Antipsychotic selection

Significant controversy exists regarding the use of 2nd generation versus 1st generation antipsychotics. Most of the data supporting no difference in efficacy between these two groups of antipsychotics comes from studies conducted in chronically ill adults with schizophrenia. Most of the controlled studies of the use of antipsychotics to treat behavioral disorders in children have been performed with 2nd generation antipsychotics, with the most evidence for risperidone. The only study comparing a 1st generation antipsychotic versus 2nd generation antipsychotics in youth was conducted in individuals with early onset schizophrenia. The 1st generation agent used in this study was molindone, an infrequently used antipsychotic that is known to be weight neutral or cause weight loss in adults. It is unknown how the results of this study can be extrapolated to the treatment of children with externalizing disorders such as conduct disorder or oppositional defiant disorders – the most common situations in which antipsychotics are prescribed in children.

Antipsychotics vary with regard to their side effect profiles, and side effects are the primary basis for individual medication choice. Second generation antipsychotics are prone to cause significant weight gain in many children, but the risk for the development of weight gain in youth varies significantly among the 2nd generation agents. In a recent study over approximately 11 weeks, the average weight gain was olanzapine (8.5kg), quetiapine (6.1 kg), risperidone (5.3 kg), and aripiprazole (4.4 kg). Olanzapine and quetiapine also caused significant increases in cholesterol and triglycerides, and risperidone increased triglycerides (Correll 2009). First generation antipsychotics are prone to causing extrapyramidal side effects. In particular, youth are especially susceptible to developing acute dystonic reactions from 1st generation antipsychotics. Similarly, 1st generation antipsychotics pose a higher risk for the development of tardive dyskinesia in chronically treated individuals. If antipsychotics are indicated, the clinician should carefully evaluate the individual needs of the child, actively engage the family in decision-making, evaluate overall benefit to risk ratio, and when indicated, choose the antipsychotic that the clinician thinks will be best tolerated by that child.

Depression, Suicidality, and Depression

In October 2003, the FDA released a public health advisory alerting health care professionals to reports of suicidality (suicidal ideation and suicide attempts) in clinical trials of antidepressants in pediatric populations. These reports provided the impetus for a FDA meta-analytic review of short-term clinical trials of antidepressants in children and adolescents. These analyses involved review, assessment, and reclassification of over 400 case descriptions. This review ultimately resulted in findings of an increased risk of suicidality during the first few weeks of antidepressant treatment. The FDA responded by issuing a *black box warning* in October 2004. The black box warning describes an increased risk of suicidality (suicidal behavior and ideation) *for ALL antidepressants* used in individuals under the age of 18. The incidence of suicidal ideations and behaviors in these pooled analyses was about 4% for those youth receiving antidepressants compared with

2% on placebo. It is important to note that no completed suicides were reported in any of these trials.

The mortality risk of depression is from suicide. Other major suicide risk factors that should be assessed include: substance abuse, conduct disorder, life stressors (such as legal or disciplinary/school problems), interpersonal losses, family and peer discord, abuse, lack of support, poor interpersonal problem-solving ability, the tendency to respond with hostility or overt aggression to frustration or stress, hopelessness and cognitive distortions. All youth with depression should be monitored carefully for the potential presence of suicidal thoughts or behaviors. This should occur at the time of initial clinical assessment and upon each visit follow-up until depression is no longer present. Assessment of suicidality should include asking questions about ideation and frequency, plans, intention, and potential dangerousness. More frequent visits, combined with follow-up calls as necessary, should be considered along with appropriate review of safety plans. It is noteworthy that in one study, the concomitant use of cognitive behavioral therapy was shown to decrease the incidence of suicidality associated with SSRI use.

Stimulants and growth

Parents and caregivers are often concerned about the possibility that stimulants may adversely affect growth. This is largely related to the fact that, at least short term, stimulants decrease appetite. Although data from different studies are mixed, results from the Multimodal Treatment of ADHD (MTA) study, indicate that weight loss occurred during the first 3-4 months of treatment, but this was followed be a resumption of weight increase. The rate of growth in height decreased by about 1-3 cm/year over the first 1-3 years of medication treatment. However, it should be noted that these decreases in height were only seen in the youth who were adherent with their stimulant medications. Although both advantages and disadvantages are associated with medication holidays or vacations, this has been suggested as one mechanism to minimize potential effects on growth. It is questionable whether the use of stimulants has any effect on ultimate adult height (Vitello 2008; Swanson 2008).

Stimulants and cardiovascular side effects

Both stimulants and atomoxetine cause small but statistically significant increases in blood pressure and pulse rate. However, it is unclear whether these changes are clinically significant. Although case reports of sudden death in children taking stimulants have been reported, a causal link has not been proven (Vitello 2008). However, a recent case control study suggests that there may be an association (Gould 2009). It is thought that underlying cardiac disorders such as serious structural abnormalities, cardiomyopathies, serious heart rhythm disturbances, or other serious cardiac problems may place children at increased risk of sudden death when stimulants are administered (FDA approved product labeling for Adderall and Concerta, 2008; Perrin 2008). The clinician should conduct a careful history of the child and the family regarding potential heart problems. A thorough physical exam should also be conducted. If the history and physical provide suspicion of a cardiac problem, then an electrocardiogram should be considered before beginning a stimulant. If the child has a known history of a cardiac problem, then a cardiology consult should be considered before beginning a stimulant (Perrin 2008).

Distinguishing between Levels of Warnings Associated with Medication Adverse Effects

Psychotropic medications have the potential for adverse effects, some that are treatment-limiting. Some adverse effects are detected prior to marketing, and are included in product labeling provided by the manufacturers. When looking at product labeling, these adverse effects will be listed in the "Warnings and Precautions" section. As well, the "Adverse Reactions" section of the product labeling will outline those adverse effects reported during clinical trials, as well as those discovered during post-marketing evaluation. Many tertiary drug information resources also report information regarding common adverse effects and precautions for use with psychotropic medications.

At times, post-marketing evaluation may detect critical adverse effects associated with significant morbidity and mortality. The Food and Drug Administration (FDA) may require manufacturers to revise product labeling to indicate these critical adverse effects. If found to be particularly significant, these effects are demarcated by a black box outlining the information at the very beginning of the product labeling, and have, in turn, been named black box warnings. Black box warnings are the strongest warning required by the FDA. It is important for clinicians to be familiar with all medication adverse effects, including black box warnings, in order to appropriately monitor patients and minimize the risk of their occurrence.

The FDA has in recent years taken additional measures to try and help patients avoid serious adverse events. New guides called Medication Guides have been developed, and are specific to particular drugs and drug classes. Medication Guides advise patients and caregivers regarding possible adverse effects associated with classes of medications, and include precautions that they or healthcare providers may take while taking/prescribing certain classes of medications. FDA requires that Medication Guides be issued with certain prescribed drugs and biological products when the Agency determines that certain information is necessary to prevent serious adverse effects, that patient decision-making should be informed by information about a known serious side effect with a product, or when patient adherence to directions for the use of a product are essential to its effectiveness. During the drug distribution process, if a Medication Guide has been developed for a certain class of medications, then one must be provided with every new prescription and refill of that medication.

Copies of the Medication Guides for psychotropic medications can be accessed on the FDA website at:

http://www.fda.gov/Drugs/DrugSafety/ucm085729.htm.

Usual Recommended Doses of Common Psychotropic Medications

The attached medication charts are intended to reflect usual doses and brief medication information of commonly used psychotropic medications. The preferred drug list of medications potentially prescribed for foster children is the same as for all other Medicaid recipients.

These are intended to serve as a guide for clinicians. The tables are not intended to serve as comprehensive drug information references or a substitute for sound clinical judgment in the care of individual patients, and individual patient circumstances may dictate the need for the use of higher doses in specific patients. In these cases, careful documentation of the rationale for the higher dose should occur, and careful monitoring and documentation of response to treatment should be observed.

Not all medications prescribed by clinicians for psychiatric diagnoses in children and adolescents are included below. However, in general, medications not listed do not have adequate efficacy and safety information available to support a usual maximum dose recommendation.

See Medication Charts beginning on page 12.

Criteria Indicating Need for Further Review of a Child's Clinical Status

The following situations indicate a need for further review of a patient's case. These parameters do not necessarily indicate that treatment is inappropriate, but they do indicate a need for further review.

For a child being prescribed a psychotropic medication, any of the following suggests the need for additional review of a patient's clinical status:

1. Absence of a thorough assessment of DSM-IV diagnosis in the child's medical record

2. Five (5) or more psychotropic medications prescribed concomitantly (side effect medications are not included in this count)

3. Prescribing of:

   (a) Two (2) or more concomitant antidepressants (if an additional one is used, may be reviewed but will be allowed if reasonable for the indications.

   (b) Two (2) or more concomitant antipsychotic medications

   (c) Two (2) or more concomitant stimulant medications[1]

   (d) Three (3) or more concomitant mood stabilizer medications

   NOTE: For the purpose of this document, polypharmacy is defined as the use of two or more medications for the same indication (i.e., specific mental disorder).

   [1] The prescription of a long-acting stimulant and an immediate release stimulant of the same chemical entity (e.g., methylphenidate) does not constitute concomitant prescribing.

   [2] When switching psychotropics, medication overlap and cross-titration may be utilized before discontinuing the first medication

4. The prescribed psychotropic medication is not consistent with appropriate care for the patient's diagnosed mental disorder or with documented target symptoms usually associated with a therapeutic response to the medication prescribed.

5. Psychotropic polypharmacy for a given mental disorder is prescribed before utilizing psychotropic monotherapy.

6. The psychotropic medication dose exceeds usual recommended doses.

7. Psychotropic medications are prescribed for children of very young age, including children receiving the following medications with an age of:

   - Antidepressants: Less than four (4) years of age
   - Antipsychotics: Less than four (4) years of age
   - Psychostimulants: Less than three (3) years of age

8. Prescribing by a primary care provider who has not documented previous specialty training for a diagnosis **other** than the following (unless recommended by a psychiatrist consultant):

   - Attention Deficit Hyperactive Disorder (ADHD)
   - Uncomplicated anxiety disorders
   - Uncomplicated depression

Members of the Ad Hoc Working Group on Psychotropic Medication Guidelines for Foster Children

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Recommendations for primary care providers on when to seek referral or consultation with a child psychiatrist can be found at http://www.aacap.org/cs/root/physicians_and_allied_professionals/when_to_seek_referral_or_consultation_with_a_child_and_adolescent_psychiatrist

Stimulants (for treatment of ADHD)

Drug	Initial Dosage	Literature Based Maximum Dosage	FDA Approved Maximum Dosage for Children and Adolescents	Schedule	Black Box Warning *	Warnings and Precautions
Amphetamine Mixed Salts *Generic available* Adderall® Adderall®XR **	5 mg/day	40 mg/day 30 mg/day-XR	Adderall approved for children 3 years and older: 40 mg/day Adderall®XR approved for children 6 years and older: 30 mg/day-XR	IR: Once or twice daily XR: Once daily	Abuse potential Sudden death and serious cardiovascular events	• Sudden death in those with pre-existing structural cardiac abnormalities or other serious heart problems • Hypertension • Psychiatric adverse event • Long-term growth suppression
Dextroamphetamine *Generic available* Dexedrine® Dexedrine Spansule®	5 mg/day	40 mg/day	Approved for children 6 years and older 40 mg/day	IR: Once or twice daily Spansule: Once daily		
Lisdexamfetamine Vyvanse®	30mg/day	70mg/day	Approved for children 6 years and older 70mg/day	Once daily		
Methylphenidate *Generic available* Ritalin® Ritalin®SR Ritalin®LA Metadate® Metadate®CD Methylin® Methylin®ER Concerta® Daytrana® TD	Ritalin IR: 10 mg/day Ritalin SR: 5 mg/day Ritalin LA: 20 mg/day Metadate: 10mg/day Methylin: 10mg/day Concerta: 18mg/day DaytranaTD: 10 mg/day	60 mg/day (30mg/day-Daytrana TD) (90mg/day-Concerta)	Approved for children 6 years and older Ritalin, Metadate, and Methylin: 60 mg/day Concerta: Children: 54 mg/day Adolescents: 72 mg/day Daytrana: 30 mg/day (largest patch)	Ritalin IR: One to three times daily Ritalin SR: Once daily Metadate: Twice daily Metadate CD: Once daily Methylin: Twice daily Methylin ER: Once daily Concerta: Once daily Daytrana TD: Once daily		
Dexmethylphenidate Focalin® Focalin® XR	5 mg/day	20 mg/day	Approved for children 6 years and older Focalin 20 mg/day Focalin XR 30 mg/day	IR: Twice daily XR: Once daily		

* See the FDA approved product labeling for each medication for the full black box warnings.

** IR, immediate-release; SR, sustained-release formulation; CD, combined immediate release and extended release; ER and XR, extended-release; TD, transdermal.

Other ADHD Treatments

Drug	Initial Dosage	Literature Based Maximum Dosage	FDA Approved Maximum Dosage for Children and Adolescents	Schedule	Baseline/ Monitoring	Black Box Warning	Warnings and Precautions
Atomoxetine Strattera®	Children: 0.5 mg/kg/day Adolescents: 40 mg/day	Children: 1.4 mg/kg/day Adolescents: 80-100 mg/day	Approved for treatment of ADHD (6-17 years) Maximum dosage should not exceed 1.4 mg/kg/day or 100 mg/day, whichever is less	Once or twice daily	None	Suicidal thinking in children and adolescents being treated for ADHD	• Liver injury • Serious cardiovascular events, including sudden death, particularly in those with pre-existing structural cardiac abnormalities or other serious heart problems • Increases in blood pressure and heart rate • Psychiatric adverse events
Clonidine *Generic available* Catapres® (immediate release) Kapvay® (extended release)	IR 0.05 mg/day ER 0.1 mg/kg/day	0.4 mg/day	Immediate release not approved for children and adolescents Extended release (brand name Kapvay®) approved for treatment of ADHD in pediatric patients (6-17 years) up to 0.4 mg/kg/day	IR: Once to four times daily ER: Once or twice daily	None	None	• Sedation • Hypotension • Do not discontinue abruptly
Guanfacine *Generic available* Tenex® (immediate release) Intuniv® (extended release)	IR 0.5 mg/day ER 0.05 mg/kg/day	4 mg/day	Immediate relase not approved for children and adolescents Extended release (brand name Intuniv™) approved for treatment of ADHD in pediatric patients (6-17 years) up to 4mg/day	IR: Once to four times per day ER: Once daily	None		
Bupropion *Generic available* Wellbutrin® Wellbutrin®SR Wellbutrin®XL	Children: 75 mg/day Adolescents: 100-150 mg/day	The lesser of:3-6 mg/kg/day OR 400 mg/day (SR) 450 mg/day (XL)	Not approved for children and adolescents	IR: Once to three times daily SR: Once to twice daily XL: Once daily	None	Increased risk of suicidal thinking and behavior (suicidality) in short-term studies in children and adolescents with major depressive disorder (MDD) and other psychiatric disorders	• Use in combination with MAOIs • Suicidal ideation • Activation of mania/hypomania • Discontinuation syndrome • Increased risk of bleeding
Imipramine *Generic available* Tofranil®	1 mg/kg/day	4 mg/kg/day OR 300 mg/day (Adolescents)	Approved for treatment of enuresis in children 6 years and older 2.5 mg/kg/day	Twice daily	• Pulse • ECG		
Nortriptyline *Generic available* Aventyl® Pamelor® Nortrilen®	0.5 mg/kg/day	2.5 mg/kg/day OR 150 mg/day (Adolescents)	Not approved for children and adolescents	Twice daily	• Pulse • ECG		

Antidepressants, SSRIs

Drug	Initial Dosage	Literature Based Maximum Dosage	FDA Approved Maximum Dosage for Children and Adolescents	Schedule	Patient Monitoring Parameters	Black Box Warning	Warnings and Precautions
Citalopram Generic available Celexa®	Children: 10-20 mg/day Adolescents: 10-20mg/day	Children: 40mg/day Adolescents: 40mg/day	Not approved for children and adolescents	Once daily	1) Pregnancy test – as clinically indicated 2) Monitor for emergence of suicidal ideation or behavior	Increased the risk of suicidal thinking and behavior (suicidality) in short-term studies in children and adolescents with major depressive disorder (MDD) and other psychiatric disorders	• Use in combination with MAOIs • Suicidal ideation • Activation of mania/hypomania • Discontinuation syndrome • Increased risk of bleeding
Escitalopram Lexapro®	Children: 5-10 mg/day Adolescents: 5-10 mg/day	Children: 20mg/day Adolescents: 20mg/day	Not approved for children Approved for Major Depressive Disorder in adolescents (12-17 years) 20 mg/day				
Fluoxetine Generic available Prozac®	Children: 10 mg/day Adolescents: 10-20 mg/day	Children: 30-60mg/day Adolescents: 60mg/day	Approved for pediatric patients 8 to 18 years For MDD 20 mg/day For OCD 60 mg/day				
Paroxetine Generic available Paxil® Paxil CR® (extended release)	Children: Not Recommended Adolescents: 10-20mg/day	Children: Not Recommended Adolescents: 40 mg/day or 37.5 mg/day for Paxil CR®	Not approved for children and adolescents				
Fluvoxamine Generic available Luvox® Luvox CR® (extended release)	Children: 25 mg/day Adolescents: 25 mg/day	Children: 200 mg/day Adolescents: 300 mg/day	Approved for treatment of OCD in chidlren (8-11 years) and adolescents (12-17) 300 mg/day				
Sertraline Generic available Zoloft®	Children: 25mg/day Adolescents: 50 mg/day	Children: 200 mg/day Adolescents: 200 mg/day	Approved for treatment of OCD in pediatric patients (6-17 years) 200 mg/day				

From Black Box Warning on package inserts: Patients of all ages who are started on antidepressant therapy should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber. Both patients and families should be encouraged to contact the clinician if depression worsens, the patient demonstrates suicidal behavior or verbalizations, or if medication side effects occur. The appropriate utilization of non-physician clinical personnel who are knowledgeable of the patient population can aid in increasing the frequency of contact between the clinic and the patient/parent.

Antidepressants, SNRIs

Drug	Starting Dose	Literature Based Maximum Dosage	FDA Approved Maximum Dosage for Children and Adolescents	Schedule	Patient Monitoring Parameters	Black Box Warning	Warnings and Precautions
Venlafaxine Extended Release Effexor XR®	Children: Insufficient Evidence Adolescents: Insufficient Evidence	Children: Insufficient Evidence Adolescents: Insufficient Evidence	Not approved for children and adolescents	Insufficient Evidence	1) Pregnancy test – as clinically indicated. 2) Blood pressure during dosage titration and as clinically necessary 3) Monitor for emergence of suicidal ideation or behavior	Increased the risk of suicidal thinking and behavior (suicidality) in short-term studies in children and adolescents with major depressive disorder (MDD) and other psychiatric disorders	• Use in combination with MAOIs • Suicidal ideation • Activation of mania/hypomania • Discontinuation syndrome • Increased risk of bleeding
Duloxetine Cymbalta®	Children: Insufficient Evidence Adolescents: Insufficient Evidence	Children: Insufficient Evidence Adolescents: Insufficient Evidence	Not approved for children and adolescents	Insufficient Evidence	1) Pregnancy test – as clinically indicated 2) Blood pressure prior to initiating treatment, during dosage titration, and as clinically indicated 3) Hepatic function testing – baseline and as clinically indicated 4) Monitor for emergence of suicidal ideation or behavior		
Desevenlafaxine Pristiq®	Children: Insufficient Evidence Adolescents: Insufficient Evidence	Children: Insufficient Evidence Adolescents: Insufficient Evidence	Not approved for children and adolescents	Insufficient Evidence	1) Pregnancy test – as clinically indicated 2) Blood pressure prior to initiating treatment, during dosage titration, and as clinically indicated 3) Hepatic function testing – baseline and as clinically indicated 4) Monitor for emergence of suicidal ideation or behavior		

From Black Box Warning on package inserts: Patients of all ages who are started on antidepressant therapy should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber. Both patients and families should be encouraged to contact the clinician if depression worsens, the patient demonstrates suicidal behavior or verbalizations, or if medication side effects occur. The appropriate utilization of non-physician clinical personnel who are knowledgeable of the patient population can aid in increasing the frequency of contact between the clinic and the patient/parent.

Antipsychotics: Second Generation (Atypical) †

Drug	Initial Dosage	Literature Based Maximum Dosage	FDA Approved Maximum Dosage for Children and Adolescents	Schedule	Patient Monitoring Parameters	Black Box Warning	Warnings and Precautions
Aripiprazole Abilify®	Children: 2.5 mg/day Adolescents: 5 mg/day	Children: 15mg/day Adolescents: 30mg/day	Approved for Bipolar Mania or Mixed Episodes in pediatric patients (10 to 17 years) and Schizophrenia in adolescents (13-17 years) 30mg/day Irritability associated with autistic disorder (6-17 years) 15mg/day	Once daily	1) CBC as indicated by guidelines approved by the FDA in the product labeling. 2) Pregnancy test – as clinically indicated 3) Weight and BMI measurement – when a new antipsychotic is initiated, at every visit (monthly for inpatients) for 6 months after the new antipsychotic is initiated, and quarterly when the antipsychotic does is stable. 4) Fasting plasma glucose level or hemoglobin A1c – before initiating a new antipsychotic, then yearly. If a patient has significant risk factors for diabetes and for those that are gaining weight – before initiating a new antipsychotic, 4 months after starting an antipsychotic, and then yearly. 5) Lipid screening [total cholesterol, low- and high-density lipoprotein (LDL and HDL) cholesterol, and triglycerides] – Every 2 years or more often if lipid levels are in the normal range, every 6 months if the LDL level is > 130 mg/dl 6) Sexual function inquiry – inquire yearly for evidence of galactorrhea/ gynecomastia, menstrual disturbance, libido disturbance or erectile/ejaculatory disturbances in males. If a patient is receiving an antipsychotic known to be associated with Prolactin elevation, then at each visit (quarterly for inpatients) for the first 12 months after starting an antipsychotic or until the medication dose is stable and then yearly 7) EPS Evaluation (examination for rigidity, tremor, akathisia) – before initiation of any antipsychotic medication, then weekly for the first 2 weeks after initiating treatment with a new antipsychotic or until the dose has been stabilized and weekly for 2 weeks after a dose increase. 8) Tardive Dyskinesia evaluation – every 12 months. For high risk patients (including the elderly), every 6 months.. 9) Vision questionnaire – ask whether the patient has experienced a change in vision and should specifically ask about distance vision and blurry vision – yearly 10) Ocular evaluations – every 2 years in youth ‡ 11) EKG – Baseline and as clinically indicated (Asenapine, Iloperidone, Paliperidone and Ziprasidone) §	Not approved for depression in under age 18. Increased the risk of suicidal thinking and behavior in short-term studies in children and adolescents with major depressive disorder and other psychiatric disorders	• Neuroleptic Malignant Syndrome • Tardive Dyskinesia • Hyperglycemia and Diabetes Mellitus • Weight gain • Akathisia • Dyslipidemia
Quetiapine Seroquel®	Children: 12.5 mg/day Adolescents: 25 mg/day	Children: 300 mg/day Adolescents: 600 mg/day	Approved Bipolar Mania (10-17 years) and for Schizophrenia in adolescents (13-17 years) 600mg/day Not approved for children	Once to twice daily			
Olanzapine Zyprexa®	Children: 2.5 mg/day Adolescents: 2.5-5 mg/day	Children: 12.5 mg/day Adolescents: 30 mg/day	Approved for Bipolar Mania or Mixed Episodes and Schizophrenia in adolescents (13-17 years) 20mg/day Not approved for children	Once to twice daily		None related to youth	
Risperidone *Generic available* Risperdal®	Children: 0.25 mg/day Adolescents: 0.5 mg/day	Children: 1.5-2 mg/day Adolescents: 2-6 mg/day	Approved for Bipolar Mania or Mixed Episodes in children and adolescents (10-17 years) and Schizophrenia in adolescents (13-17 years) 6 mg/day Irritability associated with Autistic Disorder (5-16 years) 3 mg/day	Once to twice daily		None related to youth	
Clozapine *Generic available* Clozaril® Fazaclo®	Children: 6.25-12.5 mg/day Adolescents: 6.25-25 mg/day	Children: 150-300 mg/day Adolescents: 200-600 mg/day	Not approved for children and adolescents	Once daily		Agranulocytosis; seizures; myocarditis; other adverse cardiovascular and respiratory effects	
Asenapine (sublingual) Saphris®	Insufficient Evidence	Insufficient Evidence	Not approved for children and adolescents	Insufficient Evidence		None related to youth	• Neuroleptic Malignant Syndrome • Tardive Dyskinesia • Hyperglycemia and Diabetes Mellitus • Weight gain • Akathisia • Dyslipidemia • Prolonged QTc interval
Iloperidone Fanapt®	Insufficient Evidence	Insufficient Evidence	Not approved for children and adolescents	Insufficient Evidence		None related to youth	
Paliperidone Invega®	Insufficient Evidence	Insufficient Evidence	Not approved for children and adolescents	Insufficient Evidence		None related to youth	
Ziprasidone Geodon®	Children: 10 mg/day Adolescents: 20 mg/day	Children: Insufficient Evidence Adolescents: 160 mg/day	Not approved for children and adolescents	Twice daily (Better absorbed when taken with food)		Not approved for depression in under age 18. Increased the risk of suicidality in short-term studies in children and adolescents with major depressive disorder and other psychiatric disorders	

† Dosage recommendations in this table are based on reference # 17 (Jensen, 2010).
‡ There is no current clinical consensus regarding the need for routine ocular evaluations in children and adolescents. Data from animal studies suggest that quetiapine might be associated with increased risk of cataract development, but this has not been concluded from current evidence in human use.
§ There is no current clinical consensus regarding the need for routine monitoring of QTc interval with use of Ziprasidone in children and adolescents. For additional information regarding EKG monitoring with Ziprasidone use, please refer to reference # 4 (Blair, 2005).

Antipsychotics: First Generation (Typical)

Drug	Starting Dose	Literature Based Maximum Dosage	FDA Approved Maximum Dosage for Children and Adolescents	Schedule	Black Box Warning	Warnings and Precautions
Chlorpromazine✦ *Generic available* Thorazine®	Child 0.275 mg/kg Adolescent 12.5 mg	Children younger than 5 years 40 mg/day Children 5-12 years 75mg/day Adolescent 800 mg/day	Approved for treatment of severe behavioral problems in children (6 months to 12 years) Outpatient Children: 0.25mg/pound every 4-6 hours Inpatient Children: 200mg/day in older children Adolescents 800 mg/day	Two to four times daily	None related to youth	• May alter cardiac conduction • Sedation • Orthostatic hypotension • EPS • Tardive Dyskinesia • Neuroleptic Malignant Syndrome • Use caution with renal disease, seizure disorders, respiratory disease, and any acute illness in children • Weight gain
Haloperidol✦ *Generic available* Haldol®	<35 kg: 0.25-0.5mg/day ≥35 kg: 1 mg/day	<35 kg: 3-4 mg/day ≥35 kg: 10 mg/day	Approved for treatment of Psychotic Disorders, Tourette's Disorder, and severe behavioral problems in children 3 years and older Psychosis: 0.15mg/kg/day Tourette's and severe behavioral problems: 0.075mg/kg/day 6mg/day	Once to three times daily	None related to youth	• Sedation • Orthostatic Hypotension • EPS • Photosensitivity • Tardive Dyskinesia • Constipation • Dry Mouth • Tachycardia • Prolactin elevation
Perphenazine *Generic Available* Trilafon®	≥ 12 years old 12 mg/day	6-12 years: 6 mg/day Adolescents: 64 mg/day	Approved for treatment of psychotic disorders in 12 years and older 64mg/day	Three times a day	None related to youth	• EPS • Tardive Dyskinesia • Dystonia • Neuroleptic Malignant Syndrome • Orthostatic hypotension • May alter cardiac conduction • Endocrine changes • Weight gain
Pimozide Orap®	1-2 mg/day	≤ 12 years 0.2 mg/kg/d 10 mg/day	Approved for treatment of Tourette's Disorder in 12 years and older 10mg/day	Once to twice daily	None related to youth	• EPS • Tardive Dyskinesia • Dyskinesias • Dry Mouth • Constipation • Prolactin Elevation • Prolongs QTc interval

✦Chlorpromazine and Haloperidol, when prescribed for severe behavioral problems, should be reserved for children with who have failed to respond to psychotherapy or medications other than antipsychotics.

Mood Stabilizers

Drug	Initial Dosage	Target Dose or Range	Literature Based Maximum Dosage	FDA Approved Maximum Dosage for Children and Adolescents	Schedule	Baseline Monitoring	Black Box Warning	Warnings and Precautions
Carbamazepine *Generic available* Carbatol® Tegretol® Tegretol® XR	Under 6 years: 10-20mg/kg/day 6-12 years: 100mg twice a day 12 years and older: 200mg twice a day	Under 6 years: 35mg/kg/day 6-12 years: 400-800mg/day 12 years and older: 800-1200mg/day		Approved for Seizure Disorders in all ages Maximum dosages Under 6 years: 35 mg/kg/day 6-12 years: 800mg/day 12-15 years: 1000 mg/day >15 years: 1200 mg/day	Immediate Release two to four times a day Sustained Release (XR) twice a day	• CBS • Electrolytes	Stevens-Johnson syndrome Aplastic Anemia/ Agranulocytosis	• Aplastic Anemia • Neutropenia • Hyponatremia • Induces metabolism of itself and some other drugs • Decreased efficacy of oral contraceptives • Teratogenicity • Stevens-Johnson Syndrome
Divalproex Sodium *Generic available* Depakote®	250mg/day	500mg-2000mg/day	Range: 50-120 mcg/ml Frequency: Day 7 • Weekly until stable • q6 months thereafter	Approved for Seizure Disorders in 10 years and older Maximum dose based upon serum level. Serum level: 50-100 mcg/ml or 60 mg/kg/day	Two to three times daily	• Chemistry Panel • CBC (with platelets) • LFTs • Pregnancy test	Hepatotoxicity; Teratogenicity; Pancreatitis	• Hepatotoxicity • Teratogenicity • Pancreatitis • Urea cycle disorders • Multi-organ hypersensitivity reaction • Thrombocytopenia • Withdrawal seizures • Suicidal ideation • Polycystic ovaries
Lithium *Generic available* Eskalith® Eskalith®CR Lithobid®	Children: 15-20 mg/kg/day in two to three divided doses Adolescents: 300mg three time daily (or 900mg/day)	Dose adjustment based upon serum level. Serum level: 0.4-0.6 mEq/L Note: 300mg Lithium Carbonate increases serum level by 0.2 – 0.4mEq/L	Maximum dose based upon serum level. Serum level: 0.6 – 1.2 mEq/L Frequency of blood level monitoring: • Day 7 • Weekly until stable • q3 months thereafter	Approved for manic episodes and maintenance of Bipolar Disorder in 12 years and older Maximum dose Serum level: 1.2 mEq/L	Once to three times daily	• Chemistry Panel • CBC (with platelets) • Serum Creatinine • TFTs • Pregnancy test • ECG	Toxicity above therapeutic serum levels	• Toxicity above therapeutic serum levels • Renal function impairment • Special risk patients: those with significant renal or cardiovascular disease, severe debilitation, dehydration, sodium depletion, and to patients • Polyuria • Tremor • Diarrhea • Nausea • Hypothyroid • Teratogenic
Lamotrigine *Generic Available* Lamictal®	Children: 2-5mg/day Adolescents: 25mg/day (increase by 25mg every 2 weeks)	Children: • with Valproate 1-3mg/kg/day • with Valproate and EIAED's * 1-5mg/kg/day • Monotherapy 4.5-7.5mg/kg/day • with EIAED's 5-15mg/kg/day Adolescents: • with Valproate 100-200mg/day • with Valproate and EIAED's 100-400mg/day • Monotherapy 225-375mg/day • with EIAED's 300-500mg/day		Approved for adjunctive therapy for Seizure Disorders in 2 years and older Maximum dose 500 mg/day Safety and effectiveness for treatment of Bipolar Disorder in patients below 18 years has not been established	Once to twice daily initially, then twice daily for maintenance		Serious rashes including Stevens-Johnson syndrome and asceptic meningitis	• Dermatological reactions • Potential Stevens Johnson Syndrome • Acute-multi organ failure • Withdrawal seizures • Blood dyscrasias • Hypersensitivity • Suicidal ideation

* EIAED's - Enzyme Inducing Anti-Epileptic Drugs (e.g. Carbamazepine, Phenobarbital, Phenytoin, Primidone)

Glossary

BMI = Body Mass Index. A measure of body fat based upon height and weight.

CBC = Complete blood count. Lab test used to monitor for abnormalities in blood cells, e.g., for anemia.

Serum creatinine = A lab test used to calculate an estimate of kidney function.

ECG = Electrocardiogram

EPS = Extrapyramidal side effects. These are adverse effects upon movement, including stiffness, tremor, and severe muscle spasm

FDA = U.S. Food and Drug Administration

Hemoglobin A1c = A laboratory measurement of the amount of glucose in the hemoglobin of the red blood cells. Provides a measure of average glucose over several days.

LFTs = Live function tests

MAOIs = Monoamine Oxidase Inhibitors

Prolactin = A hormone produced by the pituitary gland.

TFTs = Thyroid Function Tests

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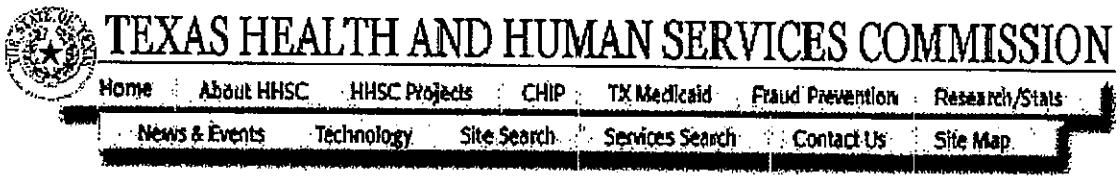

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Update on the Use of Psychoactive Medications in Texas Foster Children Fiscal Years 2002 - 2009

In June 2006, the Texas Health and Human Service Commission released a report entitled the Use of Psychoactive Medications in Texas Foster Children. The report examines the prescribing of psychoactive medications to children in foster care in terms of the Department of State Health Services (DSHS) Psychotropic Medication Utilization Parameters for Foster Children (i.e., Best Practice Guidelines) released in February 2005. The guidelines use seven criteria to indicate the need for further review of a patient's case. The report focuses on four of the seven criteria outlined in the guidelines. These are the following.

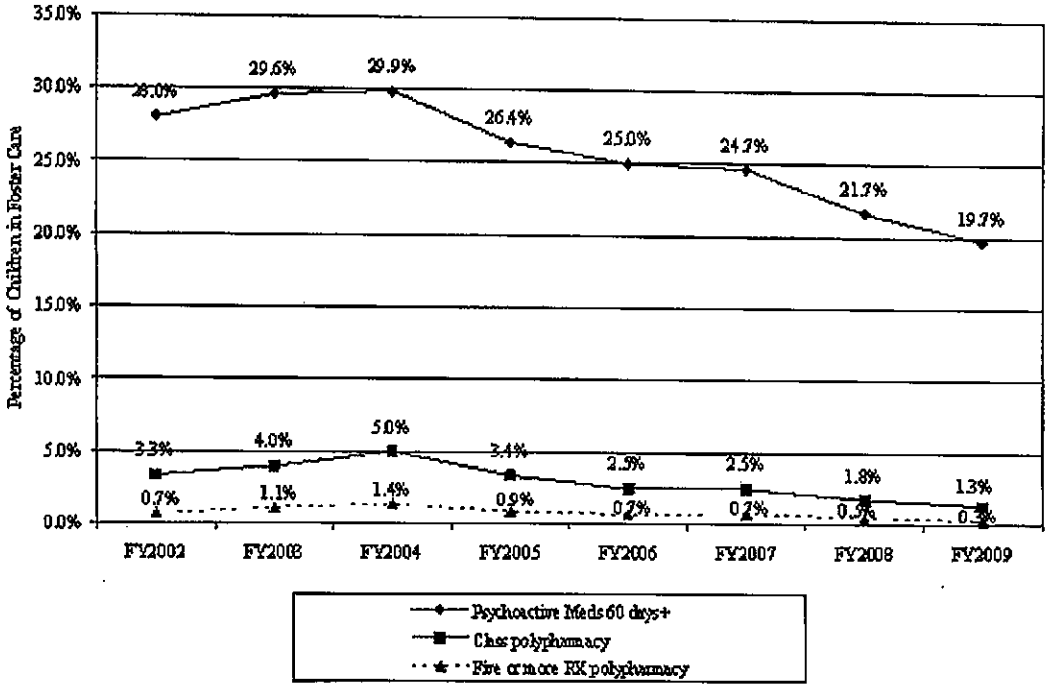
* Prescribing psychotropic medications for very young children.
* Prescribing two or more medications from the same drug class concurrently.
* Five or more psychotropic medications prescribed concurrently.
* Absence of a mental health diagnosis.

The graphs and tables below summarize key information and provide updates related to this report, which is based on Medicaid prescription and medical claims data for state fiscal years 2002 through 2009. Specifically, they show children receiving: psychoactive medications, two or more medications from the same drug class concurrently, and five or more medications concurrently. The tables provide additional information about those who received psychoactive medications and did not have a mental health diagnosis listed on Medicaid claim forms.

As the charts below show, psychoactive prescribing of all sorts have generally decreased since the release of the guidelines in early 2005 both in terms of the percentage of foster care children and in the overall number of children receiving medication.

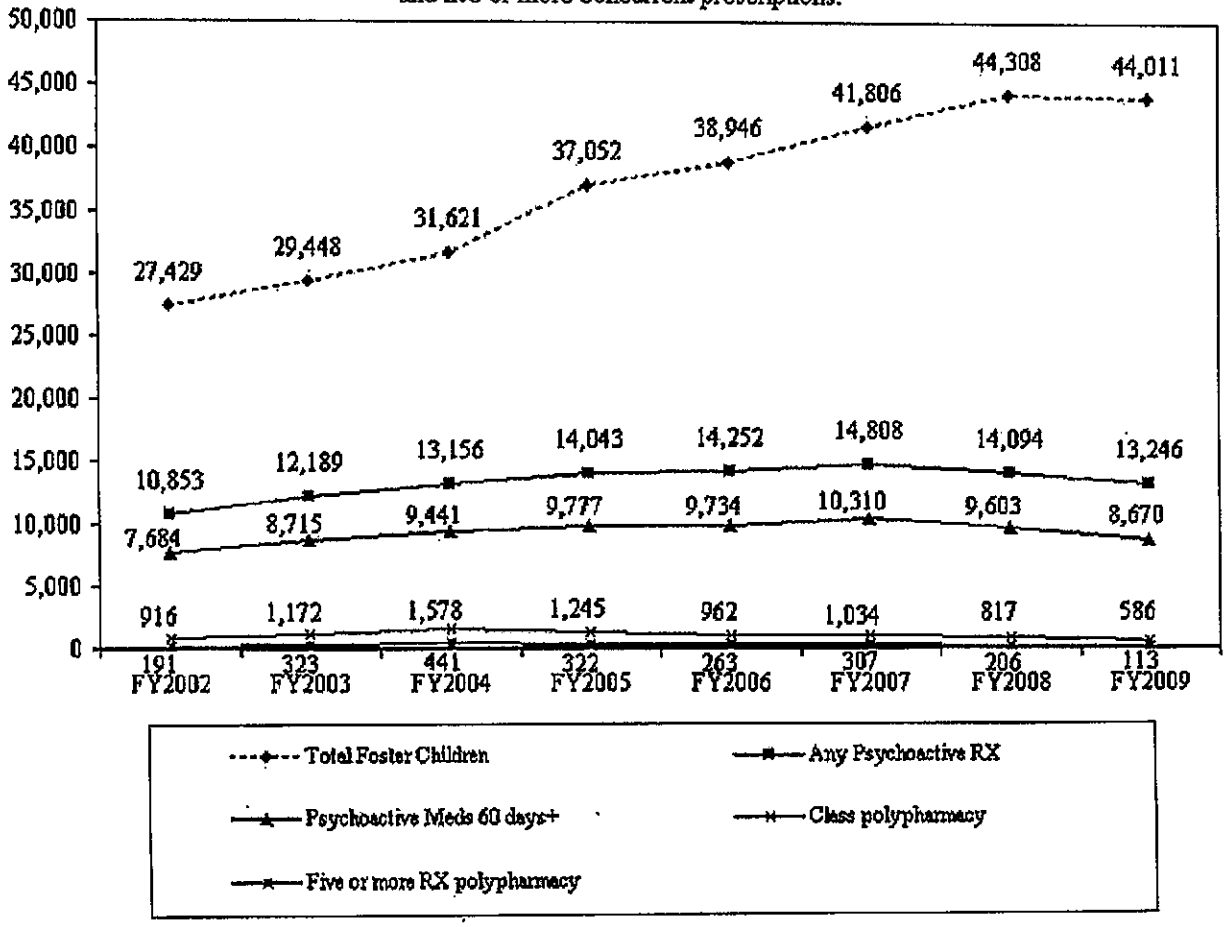
ATTACHMENT B

FY2002 to FY2009: Percentages of foster children receiving psychoactive medication for 60 days or more, two or more medications from the same class, and five or more concurrent prescriptions.



ATTACHMENT B

FY2002 to FY2009 : Total Numbers of foster children: enrolled, receiving any psychoactive medication, receiving psychoactive medication for 60 days or more, two or more medications from the same class, and five or more concurrent prescriptions.



Summary of Psychoactive Medication prescriptions for children in foster care for FY2002 through FY2009

FY2009

Age	0 – 2	%*	3	%	4 – 5	%	6 – 12	%	13 – 17	%	0 – 17	%
Total Foster children1	12,552	.	2,988	.	5,238	.	13,299	.	9,934	.	44,011	100.0%
Got psych meds2	442	3.5%	307	10.3%	1,225	23.4%	5,808	43.7%	5,464	55.0%	13,246	30.1%
Got meds ≥ 60 days3	56	0.4%	111	3.7%	652	12.4%	4,031	30.3%	3,820	38.5%	8,670	19.7%
(non-stimulant)4	.	.	63	.	.	.	.	.	.	.	63	0.1%
Class polypharmacy5	.	.	.	.	5	0.1%	199	1.5%	382	3.8%	586	1.3%
≥5 psych meds6	.	.	.	.	.	.	50	0.4%	63	0.6%	113	0.3%

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Either polypharmacy7	.	.	.	.	5	0.1%	226	1.7%	406	4.1%	637	1.4%
No MH dx (all) 8	221	1.8%	53	1.8%	131	2.5%	406	3.1%	463	4.7%	1,274	2.9%
No MH dx ≥ 60 days 9	15	26.8%	11	9.9%	42	6.4%	155	3.8%	202	5.3%	425	1.0%
(non-stimulant)	.	.	9	.	.	.	.	.	.	.	9	0.0%

FY2008

Age	0 – 2	%*	3	%	4 – 5	%	6 – 12	%	13 – 17	%	0 – 17	%
Total Foster children1	12,984	.	2,970	.	5,152	.	13,285	.	9,918	.	44,309	100.0%
Got psych meds2	417	3.2%	364	12.3%	1,388	26.9%	6,237	46.9%	5,688	57.4%	14,094	31.8%
Got meds ≥ 60 days3	63	0.5%	155	5.2%	796	15.5%	4,477	33.7%	4,112	41.5%	9,603	21.7%
(non-stimulant)4	.	.	105	.	.	.	.	.	.	.	105	0.2%
Class polypharmacy5	.	.	2	0.1%	21	0.4%	336	2.5%	458	4.6%	817	1.8%
≥5 psych meds6	.	.	.	.	3	0.1%	102	0.8%	101	1.0%	206	0.5%
Either polypharmacy7	.	.	2	0.1%	23	0.4%	368	2.8%	494	5.0%	887	2.0%
No MH dx (all) 8	185	1.4%	53	1.8%	101	2.0%	281	2.1%	263	2.7%	883	2.0%
No MH dx ≥ 60 days 9	11	17.5%	8	5.2%	30	3.8%	76	1.7%	73	1.8%	198	0.4%
(non-stimulant)	.	.	6	.	.	.	.	.	.	.	6	0.0%

HMO for foster care children started 4/1/2008

FY2007

Age	0 – 2	%*	3	%	4 – 5	%	6 – 12	%	13 – 17	%	0 – 17	%
Total Foster children1	12,160	.	2,624	.	4,740	.	12,648	.	9,634	.	41,806	100.0%
Got psych meds2	468	3.8%	401	15.3%	1,475	31.1%	6,449	51.0%	6,015	62.4%	14,808	35.4%
Got meds ≥ 60 days3	84	0.7%	170	6.5%	838	17.7%	4,687	37.1%	4,531	47.0%	10,310	24.7%
(non-stimulant)4	.	.	84	.	.	.	.	.	.	.	84	0.2%
Class polypharmacy5	.	.	5	0.2%	28	0.6%	401	3.2%	600	6.2%	1,034	2.5%
≥5 psych meds6	.	.	.	.	2	0.0%	143	1.1%	162	1.7%	307	0.7%
Either polypharmacy7	.	.	5	0.2%	29	0.6%	464	3.7%	650	6.7%	1,148	2.7%
No MH dx (all) 8	162	1.3%	43	1.6%	73	1.5%	234	1.9%	167	1.7%	679	1.6%
No MH dx ≥ 60 days 9	13	15.5%	5	2.9%	11	1.3%	64	1.4%	60	1.3%	153	1.5%
(non-stimulant)	.	.	5	.	.	.	.	.	.	.	5	0.0%

FY2006

Age	0 – 2	%*	3	%	4 – 5	%	6 – 12	%	13 – 17	%	0 – 17	%
Total Foster children1	11,327	29.1%	2,483	6.4%	4,227	10.9%	11,578	29.7%	9,331	24.0%	38,946	100.0%
Got psych meds2	377	3.3%	391	15.7%	1,350	31.9%	6,153	53.1%	5,981	64.1%	14,252	36.6%
Got meds ≥ 60 days3	61	0.5%	159	6.4%	719	17.0%	4,431	38.3%	4,364	46.8%	9,734	25.0%
(non-stimulant)4	.	.	66	.	.	.	.	.	.	.	66	0.2%

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Class polypharmacy5	.	.	2	0.10%	16	0.40%	374	3.20%	570	6.10%	962	2.50%
≥5 psych meds6	.	.	.	.	2	0.00%	120	1.00%	141	1.50%	263	0.70%
Either polypharmacy7	.	.	2	0.10%	16	0.40%	425	3.70%	619	6.60%	1,062	2.70%
No MH dx (all) 8	114	1.0%	28	1.1%	41	1.0%	140	1.2%	118	1.3%	441	1.1%
No MH dx ≥ 60 days 9	6	9.8%	3	1.9%	7	1.0%	41	0.9%	48	1.1%	105	0.3%
(non-stimulant)	.	.	3	.	.	.	.	.	.	.	3	0.0%

FY2005

Age	0 – 2	%*	3	%	4 – 5	%	6 – 12	%	13 – 17	%	0 – 17	%
Total Foster children1	11,137	30.1%	2,184	5.9%	3,896	10.5%	10,668	28.8%	9,167	24.7%	37,052	100.0%
Got psych meds2	440	4.0%	425	19.5%	1,291	33.1%	5,898	55.3%	5,989	65.3%	14,043	37.9%
Got meds ≥ 60 days3	88	0.8%	187	8.6%	743	19.1%	4,327	40.6%	4,432	48.3%	9,777	26.4%
(non-stimulant)4	.	.	83	.	.	.	.	.	.	.	83	0.2%
Class polypharmacy5	2	0.00%	1	0.00%	29	0.70%	458	4.30%	755	8.20%	1,245	3.40%
≥5 psych meds6	.	.	.	.	6	0.20%	136	1.30%	180	2.00%	322	0.90%
Either polypharmacy7	2	0.00%	1	0.00%	31	0.80%	526	4.90%	804	8.80%	1,364	3.70%
No MH dx (all) 8	133	1.2%	34	1.6%	58	1.5%	150	1.4%	154	1.7%	529	1.4%
No MH dx ≥ 60 days 9	11	12.5%	6	3.2%	18	2.4%	52	1.2%	58	1.3%	145	0.4%
(non-stimulant)	.	.	6	.	.	.	.	.	.	.	6	0.0%

DSHS best practice guidelines released in February 2005

FY2004

Age	0 – 2	%*	3	%	4 – 5	%	6 – 12	%	13 – 17	%	0 – 17	%
Total Foster children1	9,011	.	1,802	.	3,137	.	9,245	.	8,426	.	31,621	100.0%
Got psych meds2	413	4.6%	378	21.0%	1,210	38.6%	5,405	58.5%	5,750	68.2%	13,156	41.6%
Got meds ≥ 60 days3	92	1.0%	177	9.8%	705	22.5%	4,105	44.4%	4,362	51.8%	9,441	29.9%
(non-stimulant)4	.	.	73	.	.	.	.	.	.	.	73	0.2%
Class polypharmacy5	.	.	5	0.3%	37	1.2%	641	6.9%	895	10.6%	1,578	5.0%
≥5 psych meds6	.	.	.	.	5	0.2%	213	2.3%	223	2.6%	441	1.4%
Either polypharmacy7	.	.	5	0.3%	40	1.3%	712	7.7%	952	11.3%	1,709	5.4%
No MH dx (all) 8	114	1.3%	23	1.3%	57	1.8%	161	1.7%	195	2.3%	550	1.7%
No MH dx ≥ 60 days 9	8	8.7%	4	2.3%	10	1.4%	63	1.5%	92	2.1%	177	0.6%
(non-stimulant)	.	.	4	.	.	.	.	.	.	.	4	0.0%

FY2003

Age	0 – 2	%*	3	%	4 – 5	%	6 – 12	%	13 – 17	%	0 – 17	%
Total Foster children1	8,283	.	1,631	.	2,819	.	8,964	.	7,751	.	29,448	100.0%
Got psych meds2	413	5.0%	326	20.0%	1,002	35.5%	5,150	57.5%	5,298	68.4%	12,189	41.4%
Got meds ≥ 60 days3	81	1.0%	145	8.9%	604	21.4%	3,891	43.4%	3,994	51.5%	8,715	29.6%
(non-stimulant)4	.	.	79	.	.	.	.	.	.	.	79	0.3%

ATTACHMENT B

Class polypharmacy5	1	0.0%	5	0.3%	29	1.0%	409	4.6%	728	9.4%	1,172	4.0%
≥5 psych meds6	.	.	.	.	10	0.4%	158	1.8%	155	2.0%	323	1.1%
Either polypharmacy7	1	0.0%	5	0.3%	34	1.2%	487	5.4%	783	10.1%	1,310	4.4%
No MH dx (all) 8	134	1.6%	28	1.7%	51	1.8%	151	1.7%	186	2.4%	550	1.9%
No MH dx ≥ 60 days 9	18	22.2%	7	4.8%	14	2.3%	61	1.6%	91	2.3%	191	0.6%
(non-stimulant)	.	.	7	.	.	.	.	.	.	.	7	0.0%

FY2002

Age	0 – 2	%*	3	%	4 – 5	%	6 – 12	%	13 – 17	%	0 – 17	%
Total Foster children1	7,483	.	1,444	.	2,575	.	8,639	.	7,288	.	27,429	100.0%
Got psych meds2	323	4.3%	245	17.0%	831	32.3%	4,754	55.0%	4,700	64.5%	10,853	39.6%
Got meds ≥ 60 days3	63	0.8%	101	7.0%	453	17.6%	3,582	41.5%	3,485	47.8%	7,684	28.0%
(non-stimulant)4	.	.	47	.	.	.	.	.	.	.	47	0.2%
Class polypharmacy5	.	.	2	0.1%	12	0.5%	330	3.8%	572	7.8%	916	3.3%
≥5 psych meds6	.	.	.	.	5	0.2%	94	1.1%	92	1.3%	191	0.7%
Either polypharmacy7	.	.	2	0.1%	15	0.6%	367	4.2%	598	8.2%	982	3.6%
No MH dx (all) 8	112	1.5%	26	1.8%	58	2.3%	164	1.9%	205	2.8%	565	2.1%
No MH dx ≥ 60 days 9	15	23.8%	5	5.0%	16	3.5%	68	1.9%	101	2.9%	205	0.7%
(non-stimulant)	.	.	5	.	.	.	.	.	.	.	5	0.0%

*Percentages in the first row for total foster children are the percent of total foster children across that row only. All other percentages are the percent of children within a specific age group (calculated down the age group columns based on the number in that age group).

Table Notes. Data may have changed from previous versions of report due to various reasons, such as programming code changes, additional data became available, additional drugs were added to the list of psychoactive medications

1. Total children in each group is taken from the State Fiscal Year Medicaid Eligibility File and is determined by the age of the child in months at the beginning of the fiscal year. For example, zero to two includes up through the end of the 35th month after birth. Percentages across top row are percentages of total.
2. A child was considered to have gotten a psychoactive medication if any medication on the attached list was prescribed (filled and paid) at any time during the year in question. If the child got any psychoactive medication that can also be used as an anti-seizure medication or as a treatment for allergies, then the non-mental health uses of those medications was deleted from the data as much as was possible. See Methods section of the report.
3. Because many times psychoactive medications are prescribed very short term for medical illnesses (e.g. when undergoing an outpatient surgical procedure) or mental health problems (e.g. after a traumatic experience), or for psychiatric diagnoses for which they are found to be ineffective, it was decided to remove all data for children who did not receive a prescription for a psychoactive medication that lasted at least 60 days. While this may seem long, it is important to remember that prescribers tend to write 30-day or longer prescriptions even at first diagnosis. Many times these medications are not taken past a few days due to ineffectiveness, side effects, or failure to adhere to the

prescribed regimen. Therefore, it makes sense to concentrate efforts on those children who most likely were actually taking medications past an initial prescription. This row for 0 – 2 addresses the first half of Criteria 7 in the 'Criteria Indicating Need for Further Review of a Child's Clinical Status' section of the "Psychotropic Medication Utilization Parameters for Foster Children" as published on the DSHS website, hereafter referred to as the Guidelines.

4. This second line in this row shows the number of 3 year olds who got any medication for longer than 60 days that was not a stimulant medication. This item addresses the last part of Criteria 7 in the Guidelines.

5. Class polypharmacy is defined as the concurrent prescription for 60 days or longer of two unique medications from the same class. In the case of the class of mood stabilizers, where the evidence base supports the use of two meds concurrently, class polypharmacy is defined as the concurrent prescription of 3 or more meds for 60 days or longer. See the note above for an explanation of the 60-day qualifier. This row reflects Criteria 3 from the Guidelines.

6. The prescription of five or more medications concurrently is defined as any five psychoactive medications prescribed at the same time for 60 days or longer. This is a different type of polypharmacy from #5 above and is Criteria 2 from the Guidelines.

7. This row represents any child who met either of the two polypharmacy criteria of the Guidelines.

8. No MH diagnosis is defined as no ICD 9 code reflecting any mental health diagnosis listed on any claim form for services at any time during the year. The full report contains a list of diagnosis codes used.

9. No MH diagnosis >60 days is defined as no ICD 9 code reflecting any psychiatric diagnosis listed on any claim form at any time during the year for those children who received greater than 60 days of any psychoactive medication. This row addresses Criteria 1 from the Guidelines.

Use of Psychoactive Medication in Texas Foster Children State Fiscal Year 2005

Prepared by the Health and Human Services Commission, Department of State Health Services, and Department of Family and Protective Services

June 2006

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Introduction

Concerns were raised regarding the use of psychotropic medications in Texas foster children after the release of an Office of Inspector General (OIG) report in September 2004. Since then, the Texas Health and Human Services Commission (HHSC), the Department of State Health Services (DSHS), and the Department of Family and Protective Services (DFPS) have implemented a number of strategies to get a more detailed assessment of the problem and to assist providers in utilizing psychoactive medication appropriately.

In February 2005, as part of the effort to assist providers, DSHS released best practice guidelines for healthcare providers entitled *Psychotropic Medication Utilization Parameters for Foster Children.* The guidelines were developed by a panel of child and adolescent psychiatrists, psychologists, guideline development specialists, and other mental health experts for use in the treatment of foster children who receive services through Texas Medicaid. The guidelines provide parameters for the appropriate use of psychotropic medication in foster children and also alert clinicians to seven criteria, or situations, that indicate a need for further review of a patient's case. Since releasing the guidelines, State staff has worked with individual providers whose patients' medication regimens fall outside the guidelines to encourage proper prescribing.

This report outlines an additional analysis that has been done on prescribing psychoactive medication to Texas foster children for state fiscal year 2005 (September 1, 2004 through August 31, 2005). HHSC, DSHS and DFPS conducted this analysis because psychoactive medication prescribing to foster children continues to be higher on average than to other Medicaid children.

The analysis is based on Medicaid prescription and medical claims data. It includes three of the largest psychoactive drug classes (stimulants, antidepressants and antipsychotics), along with all other drug classes classified as psychotropic medications in the 2006 DSHS Formulary (e.g. mood stabilizers, sedatives/hypnotics). The DSHS Formulary is included as Appendix B.

The analysis focuses on children who received psychoactive medication for 60 or more days. Psychoactive medications initially are given on a trial basis to determine if the drug will be effective and well tolerated. Since Medicaid doctors typically write prescriptions for 30 days, one can't tell from a single claim whether a child actually took the drug for 30 days or for just a few days. For this reason, the analysis focuses on children who received psychoactive medication for 60 or more days to indicate that the child was likely on the medication beyond an initial trial period.

A full description of the methodology used in the analysis is included in the Methodology section at the end of this report.

Analysis of the Use of Psychoactive Medication in Texas Foster Children

This analysis examines psychoactive medication prescriptions for foster children in terms of DSHS' prescribing guidelines. The new prescribing guidelines use seven criteria to indicate the need for further review of a patient's case. The analysis focuses on four of the seven criteria outlined in the guidelines.

- Absence of a mental health diagnosis
- Five (5) or more psychotropic medications prescribed concurrently
- Prescribing two or more medications from the same drug class concurrently
- Prescribing psychotropic medications for very young children

The other three criteria were not explored in-depth at this time, as it may be more appropriate to analyze these data once foster children are enrolled in the new comprehensive healthcare program for foster children. These criteria are: the prescribed medication is not consistent with the patient's diagnosis; psychotropic polypharmacy for a given mental disorder is prescribed before utilizing psychotropic monotherapy; and the psychotropic medication dose exceeds usually recommended doses.

Data Summary – Foster Children

Table 1 provides a summary of psychoactive medication use in foster children in state fiscal year (FY) 2005. Of 37,052 foster children ages 0-17 who were eligible for Texas Medicaid at some point during FY 2005, 12,842 (34.7 percent) received a psychoactive medication, and 9,740 (26.3 percent) received a psychoactive medication for at least 60 consecutive days. As shown in Table 1, the use of psychoactive medication increases with age, from less than 1 percent of foster children under age 3 to 51.8 percent of foster children ages 13-17. Prescribing of psychoactive medication to foster children is much more common than prescribing to other Medicaid children, which reflects the fact that many of them have complex behavioral health care conditions and they also may be dealing with the trauma of difficult family situations and being removed from their families.

Absence of a mental health diagnosis in the child's Medicaid medical record.

Although the Medicaid claims data cannot provide information about the quality of an assessment, nor match the prescriber with the clinician making the diagnosis, it does indicate whether a psychiatric diagnosis was made at any time during the year. Service claims data was matched with prescription data in order to determine whether a child was assessed and given a mental health (MH) diagnosis during the year. See the Methodology section and Appendix A for a description of the MH diagnoses used.

Lack of a mental health diagnosis is more common in younger children and in those who were prescribed medications for less than 60 days. As noted in Table 1, slightly more than one quarter of all young children ages 2 years or younger who got any psychoactive prescriptions received no mental health diagnoses. However, the percentage with no

diagnosis was much lower for children in this age group who received 60 consecutive days or more of any psychoactive medication; only slightly more than one tenth these children received no MH diagnoses. There are a greater number of MH diagnoses for the older age groups, which reflects the higher rate of psychiatric problems as children age as well as the recognition of these problems by clinicians.

Often, prescriptions shorter than 60 days are given for non-psychiatric indications, written by non-psychiatrists, and address short-lived problems associated with other medical conditions that are more pressing or deemed primary. Prescriptions given for 60 days or longer likely represent problems perceived to be psychiatric in nature and this is reflected in the higher rate of diagnosis for this subset.

Confounding factors that would lower the apparent rate of diagnosis include the perception by some primary care clinics and practices in the community that if they list a MH diagnosis on the claim they will either not be paid or be paid at a lower rate for their service. Although this is inaccurate, this perception may limit the number of MH diagnoses. Also, many practitioners choose not to participate in the Medicaid program due to the Medicaid payment scale and administrative requirements. These practitioners may still see Medicaid patients, but if they never bill for their services, any associated diagnoses never show up in the data.

Table 3 shows the top ten most common diagnoses in each age grouping for children who received psychoactive medication for 60 days or longer.

Five or more psychotropic medications prescribed concurrently.

A total of 396 of 37,052 foster kids, or 1.1 percent, received five or more medications concurrently for a period of 60 days or longer in FY 2005. The numbers of children taking five or more medications concurrently increases with age. No children ages 0 to 3 years of age received five psychoactive medications concurrently in FY 2005, and 6 children ages 4 to 5 fell into this category. Older children are known to more commonly suffer from Bipolar Disorder and Schizophrenia, and therefore, are more likely to be prescribed five or more medications. Of the older children receiving five or more drugs at the same time, 217 were ages 13-17 and 174 were ages 6-12. The following scenario could lead to the prescription of five or more medications: A child is diagnosed with Attention Deficit Hyperactive Disorder (ADHD) and Bipolar Disorder, and is receiving a stimulant for the ADHD, lithium and another mood stabilizer for mania prophylaxis, an antidepressant for depression, and an antipsychotic for mania prophylaxis, aggression, and psychosis.

Concurrent prescribing of three or more mood stabilizers, or two or more medications from one of the following drug classes: antidepressants, antipsychotics, or stimulants.

Prescribing two or more medications from the same drug class concurrently is referred to as "class polypharmacy." As shown in Table 1, this is very uncommon for children ages 0 to 3. It becomes increasingly common in the older age groups. Table 2 lists the drug

classes for which class polypharmacy among foster children was most common. The most common class where two or more medications are prescribed concurrently are the antidepressants, which may reflect the common practice whereby the antidepressants trazodone and mirtazepine are commonly used as sleeping agents to deal with the insomnia caused by Selective Serotonin Reuptake Inhibitor (SSRI) antidepressants. When used this way, they are commonly prescribed at much lower doses than those used to treat depression. This practice is widespread and well accepted by the profession for adults, and increasingly accepted for younger patients; however the practice is not well studied. Antipsychotics are the second most commonly prescribed class involved in class polypharmacy and, although increasingly common, using two or more antipsychotics at the same time is not accepted by the experts or validated in general by the data that exists.

Prescribing of certain psychotropic medications are prescribed to very young children: antidepressants and antipsychotics to children less than 4 years old, and psychostimulants to children less than 3 years old.

Table 1 shows that of foster children ages 0-2, 86 (0.8 percent) received a psychoactive medication for 60 days or more. A child's age was determined by his/her age in months at the beginning of the fiscal year, and the 0-2 age group includes all children under age 3 (children up through the end of the 35th month after birth). Most of the 86 children in this group who received psychoactive medications were between 2 and 3 years old. The most common psychoactive medications prescribed to this age group for 60 or more days were clonidine and diphenhydramine (Benadryl), both of which were probably prescribed to treat a child who is not sleeping or whose behavior is difficult to control.

The treatment of 3 year olds with stimulants is well accepted by the medical profession. Of the 200 3-year olds who received psychoactive medications in FY 2005, 174 received a medication other than a stimulant. The most common medications prescribed to this group were clonidine and risperidone. The risperidone is likely used to treat aggression, and clonidine is probably being used to calm or help a child sleep.

Data Summary – Physicians

As noted in Table 4, there were 2,651 unique clinicians who prescribed psychoactive medication to a foster child during FY 2005. Of these clinicians, 2,110 prescribed medication for 60 days or longer. Of these 2,110 prescribers:

- 88 were associated with the 86 children ages 0 to 2 who received any psychoactive medication for 60 days or longer while 158 were associated with the similar age 3 group;
- 677 were associated with a child who was taking two or more drugs in the same class concurrently for 60 days or longer; and
- 264 were associated with a child who was prescribed five or more medications concurrently for 60 days or longer.

Table 5 provides further detail on the 264 physicians associated with a child who was prescribed five or more medications concurrently. Most of these physicians (54.2 percent) were associated with only one patient who received five or more concurrent medications; and 90 percent of them had nine patients or less on five or more concurrent meds. There were 26 physicians who were associated with 10 or more children on five or more medications concurrently. All of these physicians had psychiatric certification and/or training, and likely take care of foster children with the most complex behavioral health needs.

Trends in Prescribing Practices Since the Release of the *Psychotropic Medication Utilization Parameters for Foster Children*

DSHS released the *Psychotropic Medication Utilization Parameters for Foster Children* on February 15, 2006, almost halfway through state fiscal year 2005. In order to assess whether there were changes to prescribing patterns after the guidelines were issued, staff compared claims data five months before the release of the guidelines (September 2004 through January 2005) with five months after (April 2005 through August 2005). February and March were excluded, as these were transition months during which doctors would be adjusting their practices and clients would need time to make appointments to see their doctors after the guidelines were issued.

As Table 6 shows, psychoactive medication prescribing trends for Medicaid foster children decreased in the five months following the release of the guidelines. In particular, polypharmacy within a drug class decreased by 28.7 percent, prescribing five or more medications at the same time decreased by 30.9 percent, and prescribing to children without a mental health diagnosis decreased by 21.8 percent.

A number of factors may have contributed to the decreased trend in prescribing, including the release of the DSHS guidelines, heightened questioning of prescribing by caseworkers and judges, general media attention to the issue, and the fact that less psychiatric treatment is sought in the summer.

Discussion

It is tempting to make assumptions that these data show poor prescribing practices and children being overmedicated, however, caution needs to be exercised in singling out practitioners. The following points need to be kept in mind.

1. These patients are complex, high-risk, frequently in crisis and without detailed medical information about their diagnoses and treatments, in the company of stressed caregivers, and it takes a lot of time to successfully address their needs.
2. Few child psychiatrists accept Medicaid foster children as patients, possibly due to their complex needs along with the program's reimbursement rates and administrative requirements.

3. A relatively small number of clinicians treat these patients and if singled out they may decide not to do this work any longer.
4. Studies on changing physician prescribing behavior have regularly shown poor results with interventions focused solely on education and training. Those few studies showing impact were highly targeted and involved other practitioners (e.g. pharmacists) who question the prescribing as it happens.
5. A great deal of the prescribing may represent a lack of access to other treatments in a short timeframe, or if other treatments exist, a lack of understanding that such services are available or how to access them.
6. Good non-pharmacological treatment takes time and time is sometimes the one thing no one has because a placement is in jeopardy due to a child whose behavior is out of control.
7. Physician service patterns of all types are highly responsive to regulatory incentives that impact payment.

Next Steps

The Texas health and human services agencies will continue to work to encourage doctors to follow the prescribing guidelines for Medicaid foster children.

- The State plans to provide a summary of this data analysis to doctors who care for Texas foster children and request that they review their practices based on the analysis and the guidelines.
- The State also will focus on one or more of the criteria, such as the concurrent prescribing of five or more medications to a child. We will develop strategies to work with prescribers who meet this criterion, and especially the top 10 percent of prescribers, to better understand the specific problems they are trying to solve with so many medications and discuss possible alternative solutions.

Comprehensive Healthcare Program for Foster Care

HHSC, DFPS, DSHS and the other Texas health and human services agencies have been working together to develop a comprehensive healthcare program for foster children.

- Currently, Medicaid foster children are served through the traditional Medicaid fee-for-service model, in which they do not have a primary care physician or coordination of their physical and behavioral health care needs.
- HHSC will contract with a vendor to manage the new comprehensive healthcare program for foster children, which will be operational on or after July 1, 2007.
- Once the program is in place, one of the vendor's responsibilities will be to work with providers to encourage appropriate prescribing of psychoactive medication for foster children.

Table 1. Summary of Psychoactive Medication Use in Foster Care Children for FY 2005

Age	0 – 2	%	3	%	4 – 5	%	6 – 12	%	13 – 17	%	0 – 17	%
Total Foster kids[1]	11261	30.4 100	2196	5.9 100	3955	10.7 100	10648	28.7 100	8992	24.3 100	37052	100
Got psy meds[2]	443	3.9	424	19.3	1288	32.6	5892	55.3	5982	66.5	12842	34.7
Got meds ≥ 60 d[3] (non-stimulant)[4]	86	0.8	200 (174)	9.1 (7.9)	794	20.1	4519	42.4	4662	51.8	9740	26.3
Class poly[5]	1	0.0	3	0.1	39	1.0	569	5.3	883	9.8	1481	4.0
≥5 meds[6]	0	0	0	0	6	0.2	174	1.6	217	2.4	396	1.1
No MH dx (all)[7]	119	26.9	30	7.1	51	4.0	141	2.4	151	2.5	476	3.7
No MH dx ≥ 60d[8] (non-stimulant)	9	10.5	6 (6)	3.0 (3.4)	11	1.4	50	1.1	63	1.4	134	1.4

1. Total kids in each group is taken from the FY 2005 Medicaid Eligibility File and is determined by the age of the kid in months at the beginning of the fiscal year. For example, zero to two includes up through the end of the 35th month after birth.

2. A child was considered to have gotten a psychoactive medication if any medication on the attached list was prescribed (filled and paid) at any time during the year in question. If the child got any psychoactive medication that can also be used as an anti-seizure medication or as a treatment for allergies, then the non-mental health uses of those medications were deleted from the data as much as was possible. See Methodology section.

3. Because psychoactive medications are often prescribed in the short-term for medical illnesses (e.g. when undergoing an outpatient surgical procedure) or mental health problems (e.g. after a traumatic experience), or on a trial period for psychiatric diagnoses and not found to be effective, data for children who did not receive a prescription for a psychoactive medication that lasted at least 60 days was not included. While this may seem long, it is important to remember that prescribers tend to write 30-day or longer prescriptions even at first. Many times these medications are only taken for a few days due to ineffectiveness, side effects, or failure to adhere to the prescribed regimen. Therefore, it makes sense to concentrate efforts on those children who most likely were actually taking medications beyond an initial prescription.

4. This second line in this row shows the number of 3 year olds who got any medication for longer than 60 days that was not a stimulant medication. This item addresses the last part of Criteria 7 in the DSHS Guidelines.

5. Class polypharmacy is defined as the concurrent prescription for 60 days or longer of two unique medications from the same class as noted in Appendix B. In the case of the class of mood stabilizers, where the evidence base supports the use of two meds concurrently, class polypharmacy is defined as the concurrent prescription of 3 or more meds for 60 days or longer. See the note above for an explanation of the 60-day qualifier. This row reflects Criteria 3 from the DSHS Guidelines.

6. The prescription of 5 or more medications concurrently is defined as any five psychoactive medications prescribed at the same time for 60 days or longer. This is a different type of polypharmacy from #4 above and is Criteria 2 from the DSHS Guidelines.

7. No MH diagnosis is defined as no ICD 9 code listed on a claim form for services at any time during the year reflected any mental health diagnosis. See Appendix A for a list of diagnosis codes.

8. No MH diagnosis >60 days is defined as no ICD 9 code reflecting any psychiatric diagnosis is listed on any claim form at any time during the year for those children who received greater than 60 days of any psychoactive medication. This row addresses Criteria 1 from the DSHS Guidelines.

Table 2. Most Commonly Prescribed Class Polypharmacy in Foster Children for FY 2005*

1. Antidepressants	833 children	5. Mood stabilizers	11
2. Antipsychotics	380	6. Anxiolytics	6
3. Stimulants	236	7. Sedative/hypnotics	2
4. Miscellaneous	84		

* This counts only the last instance in the year. If a child had more than one instance of class polypharmacy, only the last instance is reflected here.

Table 3. Top 10 Most Commonly Prescribed Psychoactive Medications (≥ 60 days) + Top 10 Most Common Diagnosis Groups by Age Group

Age in yrs[1]	0-2 Medication	# 86	% 100	3 Medication	# 200	% 100	4-5 Medication	# 794	% 100	6-12 Medication	# 4519	% 100	13-17 Medication	# 4662	% 100
Top 10 Meds ≥60 d[3]	Clonidine	25	29.0	Clonidine	96	48.0	Clonidine	352	44.3	Methyphenidate	2119	46.9	Methylphenidate	1374	29.5
	Diphenhydramine	24	27.9	Risperidone	91	45.5	Risperidone	336	42.3	Risperidone	1669	36.9	Trazodone	1310	28.1
	Risperidone	21	24.4	Amphetamines	59	29.5	Amphetamines	326	42.3	Amphetamines	1605	35.5	Quetiapine	1291	27.7
	Clonazepam	9	7.0	Methylphenidate	45	22.5	Methylhenidate	305	38.4	Clonidine	1407	31.1	Risperidone	1225	26.3
	Amphetamines	8	9.3	Guanfacine	24	12.0	Quetiapine	138	17.3	Quetiapine	1103	24.4	Amphetamines	1101	23.6
	Guanfacine	8	9.3	Quetiapine	24	12.0	Atomoxetine	98	12.3	Divalproex	914	20.2	Divalproex	1101	23.6
	Hydroxyzine	8	9.3	Mirtazepine	23	11.5	Mirtazapine	98	12.3	Trazodone	712	15.8	Escitalopram	964	20.7
	Mirtazepine	8	9.3	Diphenhydramine	19	9.5	Guanfacine	86	10.8	Sertraline	701	15.6	Aripiprazole	951	20.4
	Quetiapine	7	8.1	Dexmethylphenidate	12	6.0	Divalproex	69	8.7	Atomoxetine	681	15.1	Sertraline	899	19.3
	Carbamazepine	6	7.0	oxcarbazepine	12	6.0	Trazodone	52	6.6	Aripiprazole	667	14.8	oxcarbazepine	780	16.7
	Diagnosis[2]			Diagnosis			Diagnosis			Diagnosis			Diagnosis		
Top 10 Dx	Other develop.	39	45.3	ADD	133	66.5	ADD	648	81.6	ADD	3653	80.8	ADD	2858	61.3
	Adjustment	32	37.2	Adjustment	127	63.5	Adjustment	501	63.1	Adjustment	2352	52.0	Major Dep	2046	43.9
	ADD	23	26.7	Conduct	62	31.0	PTSD's	247	31.1	Disruptive	1606	35.5	Bipolar	1969	42.2
	Speech/lang	23	26.7	Speech/lang	54	27.0	Disruptive	245	30.9	PTSD	1417	31.4	Depression NOS	1951	41.8
	Conduct	17	19.8	Disruptive	53	26.5	Conduct	164	20.7	Bipolar	1368	30.3	Adjustment Dis	1813	38.9
	Mood NOS	12	14.0	PTSD	43	21.5	Mood NOS	145	18.3	Depression NOS	1313	29.1	Disruptive	1801	38.6
	Other sleep	10	11.6	Mood NOS	37	18.5	Speech/lang	142	17.9	Major Dep.	1213	26.8	Conduct	1331	28.5
	Disruptive	9	10.5	Other develop.	36	18.0	Bipolar	138	17.4	Mood NOS	926	20.5	PTSD	1312	28.1
	Anxiety	8	9.3	Bipolar	25	12.5	Depression NO	122	15.4	Conduct	823	18.2	Mood NOS	1058	22.7
	Coordination	8	9.3	Depression NOS	23	11.5	Anxiety	96	12.1	Anxiety	542	12.0	Dysthymic	820	17.6

Age in yrs[1]	0-17 Medication	# 9740	% 100
Top 10 Meds ≥60 d[3]	Methylphenidate	3697	38.0
	Risperidone	3201	32.9
	Amphetamines	2979	30.6
	Quetiapine	2475	25.4
	Clonidine	2459	25.2
	Trazodone	2034	20.9
	Divalproex	2023	20.8
	Aripiprazole	1621	16.6
	Sertraline	1600	16.4
	escitalopram	1478	15.2
	Diagnosis		
Top 10 Dx	ADD	6891	70.7
	Adjustment	4576	47.0
	Disruptive	3508	36.0
	Bipolar	3331	34.2
	Depression NOS	3260	33.5
	Major Depression	3165	32.5
	PTSD	2853	29.3
	Conduct	2277	23.4
	Mood NOS	2058	21.1
	Dysthymic	1251	12.8

1 Child in months at the beginning of the fiscal year. 2 See Appendix A for listing of ICD-9 Codes included in each diagnosis group.

Table 4. Summary of Physicians Prescribing Psychoactive Medication to Foster Children

Age (yrs)[1]	0-2	%	3	%	4-5	%	6-12	%	13-17	%	Total	%
Prescribing any[2]	353	100	270	100	630	100	1582	100	1467	100	2651	100
Pres ≥60 d[3]	88	24.9	158	58.5	461	72.2	1329	84.0	1231	83.9	2110	79.6
Class poly[4]	2	0.6	9	3.3	56	8.9	374	23.6	481	32.8	677	25.5
≥5 meds[5]	0	0	0	0	16	2.5	155	9.8	171	11.7	264	10.0
Total poly[6]	2	0.6	9	3.3	60	9.5	397	25.1	490	33.4	698	26.3

1. Child in months at the beginning of the fiscal year. For example, zero to two includes up through the end of the 35th month after birth.
2. The number of clinicians who wrote any prescription of a psychoactive medication for a child in the age group listed.
3. The number of clinicians associated with children who received any psychoactive medication prescription for 60 or more days.
4. The number of clinicians associated with the group of children who received 2 psychoactive medications from the same class for 60 or more days.
5. The number of clinicians associated with the group of children who received 5 or more psychoactive medications concurrently for 60 days or more.
6. The total number of clinicians associated with polypharmacy of either 2 or more drugs from the same class or prescribing 5 or more medications concurrently. It is not a sum of the previous 2 rows as there is overlap between the two groups.

Table 5. Physicians with Patients on Five or More Psychoactive Medications Concurrently

# of patients	# of doctors	%	Cumulative freq	Cumulative %
1	143	54.2	143	54.2
2	36	13.6	179	67.8
3	24	9.1	203	76.9
4	7	2.7	210	76.9
5	12	4.6	222	84.1
6	6	2.3	228	86.4
7	5	1.9	233	88.6
8	1	0.4	234	88.6
9	4	1.5	238	90.2
10*	1	0.4	239	90.5
11	2	0.8	241	91.3
12	1	0.4	242	91.7
14	1	0.4	243	92.1
15	2	0.8	245	92.8
16	2	0.8	247	93.6
17	1	0.4	248	93.9
19	3	1.1	251	95.1
20	2	0.8	253	95.8
21	3	1.1	256	97.0
22	2	0.8	258	97.7
27	1	0.4	259	98.1
28	1	0.4	260	98.5
29	1	0.4	261	98.9
32	2	0.8	263	99.6
60	1	0.4	264	100.0

* 238 doctors (90% of this group) had 9 or fewer patients on 5 or more psychoactive medications concurrently, while 26 doctors (10%) had 10 or more patients.

Table 6. Comparison of Psychoactive Medication Prescribing to Foster Children Before and After the Release of the DSHS Guidelines

	5 Months Prior to the Guidelines 9/1/04 to 1/31/05		5 Months After the Guidelines 4/1/05 to 8/31/05		
	Ages 0-17	**Percent**	**Ages 0-17**	**Percent**	**Percent Change**
Total children in foster care	27,391*		30,491*		**+11.3%**
Got a psychoactive medication	9,894	36.12%	10,257	33.64%	**-6.9%**
Got a psych med for 60 or more days	7,005	25.57%	7,127	23.37%	**-8.6%**
2+ drugs in same class at same time	862	3.15%	684	2.24%	**-28.7%**
5 or more meds at same time	204	0.74%	157	0.51%	**-30.9%**
No MH diagnosis for those w/ a psych med for 60 or more days	171	2.44%	136	1.91%	**-21.8%**

*Of these children, 20,995 were in foster care both before and after the guidelines were issued.

Methodology

Data Source files

The analysis utilized the 2005 Medicaid eligibility, vendor drug prescriptions and Medicaid acute care (inpatient and non-inpatient) claims files for foster children (i.e. children with type programs 08, 09, or 10). All foster children for whom the state is the guardian receive Medicaid type programs 08, 09, or 10. A type program indicator is included in the eligibility file, but not the vendor drug file, so the eligibility file has to be matched with the drug file to pull back appropriate claims. Only claims and prescriptions for foster care type programs 08, 09, or 10 during the year were selected.

Medicaid Eligibility file

The Medicaid 8-month eligibility file is a final cleaned file of Medicaid eligibility and enrollment available approximately 8 months after any particular eligibility month. The enrollment file contains personal identification information (e.g., name, birthday), demographics, and Medicaid enrollment information. The final FY 2005 8-month eligibility file was used to determine the complete list of foster care children enrolled in type programs 08, 09, or 10 during FY2005.

Medicaid Vendor Drug file

The vendor drug claims files consist of all the paid (not written, or filled) vendor drug prescriptions for Medicaid during a particular month. Within a fiscal year, it is estimated that over 98 percent of all prescriptions, written or filled, are paid. The information in the vendor drug file is limited to that information typically seen on a prescription by a patient and pharmacist with some additional Medicaid payment information; there is no diagnostic information included in the file. The vendor drug file contains limited information on demographics and eligibility enrollment and extensive information on drugs prescribed, type of drug, amount paid, prescription, fill and payment dates. The identifying information for doctors in the vendor drug file is the Texas license number.

Medicaid Acute Care Claims files

The Medicaid acute care claims files (inpatient hospital, outpatient hospital, outpatient physician/suppliers) contain extensive information on Medicaid procedures performed, amounts paid, diagnoses, dates of service, payment dates, and provider information, and limited information on demographics and eligibility enrollment. All diagnoses are based on the ICD 9 (International Classification of Diseases) and all procedures are based on the Current Procedural Technology (CPT) codebook. The identifying information for doctors in the Medicaid acute care claims files is the Medicaid provider ID, and not the Texas license number.

Each individual in Medicaid has a unique Patient Control Number (PCN) that is located on all claims. The PCN was used to match individuals' prescriptions and claims. Because

the identifying information for doctors differs across the files and the crosswalk tables between Medicaid provider IDs and Texas license numbers are incomplete, it is not possible to match individual physician's prescriptions and claims diagnostic and service information with any degree of accuracy.

Programming

1. Appropriate prescriptions were identified: All foster children who were in a particular age group based on their age at the fill date were selected from the vendor drug file. Only prescriptions filled for foster children during their months of foster care program enrollment during the fiscal year were retained for analysis.
2. Corresponding medical claims for these individuals were identified: claims in the acute care claims files for foster children from step 1 were identified using PCNs.
    a. All individual diagnoses were also coded into a set of ICD 9 groups (such as "Depression", "Schizophrenia", etc). See Appendix A for a summary of the ICD 9 diagnosis groups.
    b. Every mental health diagnosis from the five available diagnoses fields was identified.
    c. All unique mental health diagnoses for each client were identified; only a single instance of each unique diagnostic group was kept for each client.
    d. All diagnoses between ICD-9 codes 290 and 319 were identified as Mental Health diagnoses.
    e. All seizure diagnoses from the five available diagnoses fields were identified.
    f. All unique seizure diagnoses for each client were identified; only a single instance of each unique diagnosis was kept for each client.
    g. All unique allergy diagnoses for each client were identified; only a single instance of each unique diagnosis was kept for each client.
    h. The end result is basically a record of every unique MH diagnosis within the defined ICD 9 diagnostic groups for each client.
3. Seizure client drug subsets were removed: three separate screening procedures were used to remove clients whose seizure diagnoses and prescriptions indicated that the prescriptions being utilized were most likely being prescribed for seizures, rather than mental health purposes.
    a. Potential dual use drugs were identified as: Carbamazepine, Diazepam, Gabapentin, Lamotrigine, Oxcarbazepine, Topiramate, Divalproex Sodium,Valproate Sodium,Valproic Acid
    b. Seizure diagnoses were identified as shown in Appendix D.
    c. Stage 1: All clients who had seizure diagnoses in the claim file and were receiving possible dual use MH/seizure drugs were identified. For all these clients three separate screens were enacted:
        i. Screen 1: If the clients had no other MH drug prescriptions, and they had no other mental health diagnoses, they were deleted from the sample. (e.g. the only thing this group was receiving were dual

use MH/seizure drugs and the only diagnoses they had were for seizures).

ii. Screen 2: If the clients had no other MH drug prescriptions, and they had one or more MH diagnoses but they did NOT have a Bipolar Disorder diagnosis, then they were deleted from the sample.

iii. Screen 3: If the clients did have other MH drug prescriptions, and they had one or more MH diagnoses but they did NOT have a Bipolar Disorder diagnosis, then ONLY the dual use MH/seizure drugs prescriptions and the seizure disorders were deleted from the sample. For these clients all their other non-seizure drugs and diagnoses were retained in the data file for analysis.

4. Allergy and skin condition client drug subsets were removed: Diphenhydramine and Hydroxyzine were identified as dual use mental health/allergy medications.
   a. A list of allergy and skin condition diagnoses was compiled from the ICD 9. A list of the diagnoses found in the data set that were identified among foster care children is provided in Appendix C.
   b. If a client had no mental health diagnoses (e.g. nothing between ICD-9 290 and 319) and no mental health drug prescriptions (e.g. no prescriptions other than Diphenhydramine and Hydroxyzine), and a client did have an allergy diagnosis (listed in Appendix C) and the client did have an allergy prescription (Diphenhydramine or Hydroxyzine); then those clients were deleted from the drug file and the claims file.
5. Five or more concurrent prescriptions for 60 days were identified: for the remaining drugs in the vendor drug file an array was created consisting of every generic drug that every patient had for every day during the year.
   a. For every day of the year the total number of prescriptions open for each individual generic drug were counted for each patient.
   b. Each prescription's start date was defined as the fill date on the claim and the end date as the fill date plus the days supply listed on the claim.
   c. For each patient's different specific generic drug prescriptions, each day of the year was recoded to indicate only the presence or absence of a particular generic drug prescription being open on that day.
   d. Generic drug prescriptions for clients whose total number of days during the year were less than 60 were deleted.
   e. The array was then rolled up to the level of clients by summing the number of active generic drug prescriptions for all generic drugs a client had for every day of the year.
   f. All clients who had less than 4 generic drug prescriptions during the entire year were deleted.
   g. For the remaining clients every day of the year that had 4 or fewer prescriptions open on it was coded as a 0 (zero). All days that had 5 or more prescriptions open on it were coded as a 1 (one).
   h. Every continuous 60-day block of the year was examined; if the sum of the days was 60 then the client was flagged as meeting the criteria of 5 or more concurrent psychotropic prescriptions and the starting day of that

period was noted. Because the program processed the file continuously from the beginning to the end of the year, only the last 60-day period in which a client had 5 or more prescriptions open for 60 consecutive days was retained.

6. Two or more concurrent prescriptions (three or more for mood stabilizers) within the same DSHS Formulary Class for 60 days were identified. A similar procedure was used to identify clients who had concurrent prescriptions open within the same drug class for 60 days or more.
    a. Every day of the year a binary indicator was computed for each specific generic drug for each patient (steps 4a – 4d above).
    b. However, unlike the previous analysis, instead of rolling up to the level of the client, the drugs were rolled up to the combined level of the client and DSHS drug formulary classes.
    c. Clients' specific formulary classes that had only a single generic drug prescription in a formulary class during the year were deleted. The clients that had only 2 or fewer generic drug prescriptions from the mood stabilizer formulary class during the year were deleted.
    d. A binary recoding was then performed in order to count the days on which clients had 2 or more (3 or more for mood stabilizers) open prescriptions for every day of the year. Similar to the previous method (step 4h above), every continuous 60-day block during the year was examined for the presence of 2 or more (3 or more for mood stabilizers) open generic drug prescriptions within each DSHS drug formulary class a client had. The last 60 days that a client met the criteria for open concurrent prescriptions within a DSHS drug formulary class for each drug class combination was flagged and retained.
7. Clients who had received any generic drug prescription for 60 days or more were identified; a similar procedure to that described above for concurrency was used to identify clients who had any generic drug prescriptions open for 60 days or more. Clients who meet the criteria's records were flagged and retained.
8. Clients meeting the concurrency criteria had their claims and prescriptions records flagged for analysis. All the clients whose records were flagged and retained from the five (5) or more concurrent prescriptions during 60 days analysis or concurrent generic drug prescriptions within DSHS formulary classes were merged back into the original file in order to pull out all of their prescription and claims records.
9. This file of prescriptions and diagnoses for foster children who met one of the two criteria for concurrent prescriptions formed the basic file for most analyses. Some additional analyses used the total prescriptions or all claims for all foster children. The prescriptions and diagnostic records were then analyzed using SAS and SQL to produce the summary tables.

Appendix A
Defining ICD 9 Codes for Mental Health ICD 9 Groups

Group Name	Start ICD Diagnosis Code	End ICD Diagnosis Code
Dementia	290	29099
Alcohol	291	29199
Other Drug	2920	29299
Mental Disorder Due To GMC	293	29399
Misc. Cognitive Disorders	294	29499
Schizophrenia	29500	29599
Bipolar	2960	29619
Major Depression	29620	29639
Bipolar	29640	29689
Mood Disorder NOS	29690	29699
Other Psychotic	2970	29899
PDD	299	29980
Other Psychotic	29999	29999
Anxiety	300	
Anxiety	30002	
Anxiety	30009	
Factitious Disorders	30016	30019
Phobias	30020	30029
OCD	3003	
Dysthymic	3004	
Neurasthenia	3005	
Depersonalization	3006	
Body Dysmorhphia / Hypocondriasis	3007	
Somatoform	30081	30089
Unspecified Mental Disorder	3009	
Personality Disorder	301	30199
Psychosexual Disorders	3022	3029
Alcohol	303	30399
Other Drug	304	30599
Sexual Disorders	30651	
Hysteria	3060	3069
Stuttering	307	
Eating Disorder	3071	
Tic Disorders	3072	3073
Sleep Disorders	30740	30749
Eating Disorder	30750	30759
Elimination Disorders	3076	3077
Pain Disorders	3078	30789
Communication/Habit Disorder	3079	

Group Name	Start ICD Diagnosis Code	End ICD Diagnosis Code
Adjustment Disorder	3080	3094
PTSD	30981	30989
Adjustment Disorder	3099	
Mental Disorder Due To Brain Damage	310	3109
Depression NOS	311	
Impulsive Disorders	31230	31239
Conduct	3120	31229
Conduct	3124	3129
Anxiety	3130	
Dysthymic	3131	
Disruptive	3133	31381
Social Withdrawal	3121	3123
Identity	31382	
Academic Disorders	31383	
Reactive Attachment	31389	
Childhood Mental Disorder NOS	3139	
ADD	314	31499
Academic Disorders	315	3152
Academic Disorders	3159	
Speech Language	31531	31539
Coordination	3154	
Other Developmental	3155	3159
Psychic Factors With GMC	316	
MR	317	319
Movement Disorders	3321	33399
Narcolepsy	347	
Other Sleep Disorders	7805	78059
Elimination Disorders	7876	

Appendix B
DSHS Formulary Classes and Generic Drug Names

DSHS FORMULARY	Generic Name
ANTIDEPRESSANTS	Amitrip Hcl/Chlordiazepoxide
ANTIDEPRESSANTS	Amitriptyline Hcl
ANTIDEPRESSANTS	Amitriptyline Hcl/Perphenazine
ANTIDEPRESSANTS	Amoxapine
ANTIDEPRESSANTS	Bupropion Hcl
ANTIDEPRESSANTS	Citalopram Hydrobromide
ANTIDEPRESSANTS	Desipramine Hcl
ANTIDEPRESSANTS	Doxepin Hcl
ANTIDEPRESSANTS	Duloxetine Hcl
ANTIDEPRESSANTS	Escitalopram Oxalate
ANTIDEPRESSANTS	Fluoxetine Hcl
ANTIDEPRESSANTS	Fluvoxamine Maleate
ANTIDEPRESSANTS	Imipramine Hcl
ANTIDEPRESSANTS	Imipramine Pamoate
ANTIDEPRESSANTS	Mirtazapine
ANTIDEPRESSANTS	Nortriptyline Hcl
ANTIDEPRESSANTS	Paroxetine Hcl
ANTIDEPRESSANTS	Paroxetine Mesylate
ANTIDEPRESSANTS	Phenelzine Sulfate
ANTIDEPRESSANTS	Sertraline Hcl
ANTIDEPRESSANTS	Trazodone Hcl
ANTIDEPRESSANTS	Tranylcypromine Sulfate
ANTIDEPRESSANTS	Trimipramine Maleate
ANTIDEPRESSANTS	Venlafaxine Hcl
ANTIPSYCHOTICS	Aripiprazole
ANTIPSYCHOTICS	Chlorpromazine Hcl
ANTIPSYCHOTICS	Clozapine
ANTIPSYCHOTICS	Fluphenazine Decanoate
ANTIPSYCHOTICS	Fluphenazine Hcl
ANTIPSYCHOTICS	Haloperidol
ANTIPSYCHOTICS	Haloperidol Decanoate
ANTIPSYCHOTICS	Haloperidol Lactate
ANTIPSYCHOTICS	Loxapine Succinate
ANTIPSYCHOTICS	Mesoridazine Besylate
ANTIPSYCHOTICS	Molindone Hcl
ANTIPSYCHOTICS	Olanzapine
ANTIPSYCHOTICS	Olanzapine/Fluoxetine Hcl
ANTIPSYCHOTICS	Perphenazine

DSHS_FORMULARY	Generic_Name
ANTIPSYCHOTICS	Quetiapine Fumarate
ANTIPSYCHOTICS	Risperidone
ANTIPSYCHOTICS	Risperidone Microspheres
ANTIPSYCHOTICS	Thioridazine Hcl
ANTIPSYCHOTICS	Thiothixene
ANTIPSYCHOTICS	Trifluoperazine Hcl
ANTIPSYCHOTICS	Ziprasidone Hcl
ANTIPSYCHOTICS	Ziprasidone Mesylate
ANXIOLYTICS	Alprazolam
ANXIOLYTICS	Buspirone Hcl
ANXIOLYTICS	Chlordiazepoxide Hcl
ANXIOLYTICS	Clonazepam
ANXIOLYTICS	Clorazepate Dipotassium
ANXIOLYTICS	Diazepam
ANXIOLYTICS	Lorazepam
ANXIOLYTICS	Oxazepam
MISCPSYCH	Clomipramine Hcl
MISCPSYCH	Clonidine Hcl
MISCPSYCH	Gabapentin
MISCPSYCH	Guanfacine Hcl
MISCPSYCH	Propranolol Hcl
MOOD STABILIZERS	Carbamazepine
MOOD STABILIZERS	Divalproex Sodium
MOOD STABILIZERS	Lamotrigine
MOOD STABILIZERS	Lithium Carbonate
MOOD STABILIZERS	Lithium Citrate
MOOD STABILIZERS	Oxcarbazepine
MOOD STABILIZERS	Topiramate
MOOD STABILIZERS	Valproate Sodium
MOOD STABILIZERS	Valproic Acid
MOOD STABILIZERS	Verapamil Hcl
SEDATIVES-HYPNOTICS	Chloral Hydrate
SEDATIVES-HYPNOTICS	Diphenhydramine Hcl
SEDATIVES-HYPNOTICS	Hydroxyzine Hcl
SEDATIVES-HYPNOTICS	Hydroxyzine Pamoate
SEDATIVES-HYPNOTICS	Temazepam
SEDATIVES-HYPNOTICS	Triazolam
SEDATIVES-HYPNOTICS	Zaleplon
SEDATIVES-HYPNOTICS	Zolpidem Tartrate

DSHS FORMULARY	Generic Name
STIMULANTS	Amphet Asp/Amphet/D-Amphet
STIMULANTS	Atomoxetine Hcl
STIMULANTS	D-Amphetamine Sulfate
STIMULANTS	Dexmethylphenidate Hcl
STIMULANTS	Methylphenidate Hcl

Appendix C
Seizure Diagnosis Codes

ICD 9 Diagnosis Code	Description
3332	Myoclonus
34500	Gen Noncv Ep W/O Intr Ep
34501	Gen Nonconv Ep W Intr Ep
3451	Gen Cnv Epil W W/O Intr E
34510	Gen Cnv Epil W/O Intr Ep
34511	Gen Cnv Epil W Intr Epil
3452	Petit Mal Status
3453	Grand Mal Status
34540	Psymotr Epil W/O Int Epi
34541	Psymotr Epil W Intr Epil
34550	Part Epil W/O Intr Epil
34551	Part Epil W Intr Epil
3456	Inf Spasm W W/O Intr Epil
34560	Inf Spasm W/O Intr Epil
34561	Inf Spasm W Intract Epil
34570	Epil Par Cont W/O Int Ep
3458	Epilep Nec W W/O Intr Epi
34580	Epilep Nec W/O Intr Epil
34581	Epilepsy Nec W Intr Epil
3459	Epilep Nos W W/O Intr Epi
34590	Epilep Nos W/O Intr Epil
34591	Epilepsy Nos W Intr Epil
7803	Convulsions
78030	Convulsions
78031	Febrile Convulsions
78039	Convulsions Nec

Table above lists all seizure diagnoses found among the sample of FY05 foster care children.

Appendix D
Allergy and Skin Conditions Diagnoses Codes

ICD 9 Diagnosis Code	Description
33381	Blepharospasm
33382	Orofacial Dyskinesia
33383	Spasmodic Torticollis
33390	Extrapyramidal Dis Nos
33399	Extrapyramidal Dis Nec
4770	Rhinitis Due To Pollen
4771	Allergic Rhinitis-Food
4772	
4778	Allergic Rhinitis Nec
4779	Allergic Rhinitis Nos
69010	Sebrrheic Dermatitis Nos
69011	Seborrhea Capitis
69018	Sebrrheic Dermatitis Nec
6910	Diaper Or Napkin Rash
6918	Other Atopic Dermatitis
692	
6920	Detergent Dermatitis
6921	Oil & Grease Dermatitis
6922	Solvent Dermatitis
6923	Topical Med Dermatitis
6924	Chemical Dermatitis Nec
6925	Topical Food Dermatitis
6926	Dermatitis Due To Plant
69270	Solar Dermatitis Nos
69271	Sunburn
69272	Act Drmtitis Solar Rdiat
69276	Sunburn Of Second Degree
69283	Dermatitis Metals
69289	Dermatitis Nec
6929	Dermatitis Nos
6960	Psoriatic Arthropathy
6961	Other Psoriasis
6962	Parapsoriasis
6963	Pityriasis Rosea
6965	Pityriasis Nec & Nos
6968	Psorias Related Dis Nec
698	
6980	Pruritus Ani
6981	Pruritus Of Genitalia

6982	Prurigo
6983	Lichenification
6984	Dermatitis Factitia
6988	Pruritic Conditions Nec
6989	Pruritic Disorder Nos
7051	Prickly Heat
70581	Dyshidrosis
70583	Hidradenitis
70589	Sweat Gland Disorder Nec
7060	Acne Varioliformis
7061	Acne Nec
7062	Sebaceous Cyst
7063	Seborrhea
7068	Sebaceous Gland Dis Nec
7069	Sebaceous Gland Dis Nos
7080	Allergic Urticaria
7081	Idiopathic Urticaria
7083	Dermatographic Urticaria
7088	Urticaria Nec
7089	Urticaria Nos
7098	Skin Disorders Nec
7099	Skin Disorder Nos
7821	Nonspecif Skin Erupt Nec

Table above lists all allergy and skin condition diagnoses found among the sample of FY05 foster care children.

APPENDIX C

Multi-State Project "Children getting Anti-psychotics": Texas State Summary and Recommendations on Antipsychotic[1] and Mental Health Drugs[2] Utilization and Trends (2004-2007) in Medicaid Children and Foster Care

- *Total Users:* 46,072 children and adolescents had a prescription filled for an antipsychotic (AP) medication in 2007.
  - *Trend:* AP use in children and adolescents increased 16%, based on comparisons of data from 2004 to 2007.
- *AP Use in the Very Young:* 5,143 children less than or equal to 5 years of age had a prescription filled for an AP medication in 2007.
- *High Dose:* 896 children and adolescents had prescriptions filled for high doses[3] of selected AP medications in 2007.
- *Multiple AP Use:* 8,714 children and adolescents had prescriptions filled for two or more AP medications in 2007.
- *Multiple Mental Health Drugs:* 17,713 children and adolescents had prescriptions filled for four or more MHDs in 2007.
- *Adherence:* 17,298 children and adolescents had a >20-day gap between having their AP medications filled in 2007.

Executive Summary and Recommendations: There are **two important caveats** to looking at the numbers and rates between States. **First**, each State had differing eligibility criteria, which affects the proportion of the general child population covered, as well as the number of children classified as Aged, Blind, and Disabled, or as having special health needs. States also have differing percentages of managed care, capitation, and fee for service. The project was not able to risk adjust therefore variations among States may in part be due to differences in underlying populations. Comparisons should be reviewed with a view towards further investigation at the local level to determine what prescriber or systemic factors may affect variation. **Second**, most States had one or more rates that were high and one or more rates that were low, suggesting potentially avoidable variation in the delivery of care. This offers participant States the opportunity to learn from each other to inform policies, practices, and systems and to develop shared processes for collecting data. The following recommendations offer a road map of where to begin, review, and seek potential solutions:

- In 2007 among children under 19 years of age, areas that had rates in the lowest quartile included:
  - Gaps in AP therapy of greater than 20 days in foster care children.
  - Texas State should consider sharing processes with others
- In 2007 among children under 19 years of age, areas that had rates in the middle two quartiles included:

[1] AP refers to first- and second-generation antipsychotic medications.
[2] MHD is an abbreviation for "mental health drugs".
[3] High does thresholds are based on Texas guidelines. For 5 year olds, "high dose" is defined as greater than the Texas maximum dose; and for 6 to 18 year olds, "high dose" is defined as more than 2 times the Texas maximum dose. *Use of Texas of Psychoactive Medication in Texas Foster Children State Fiscal Year 2005.* Prepared by the Health and Human Services Commission, Department of State Health Services, and Department of Family and Protective Services. June 2006.Washington

- Rates of overall AP use, AP use in those 5 years of age and younger, children prescribed high doses of APs, use of 2 or more APs, and use of 4 or more MHDs.
- Trends and issues may or may not need further analysis

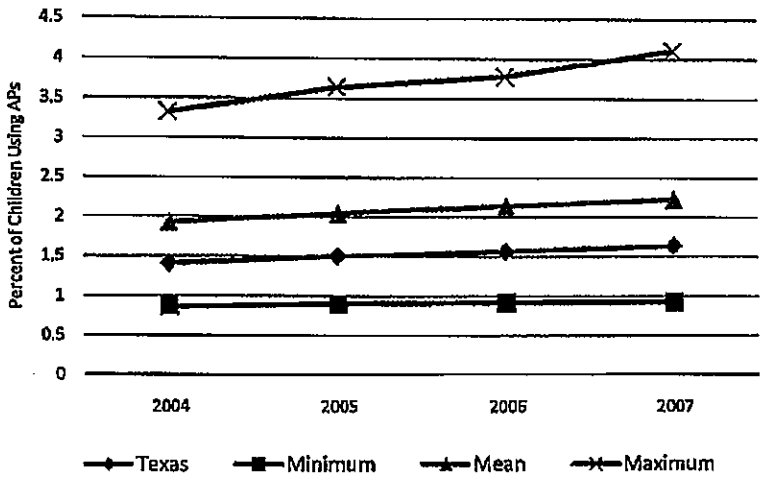
- In 2007 among children under 19 years of age, areas that had rates in the highest quartile included:
  - Gaps in AP therapy of greater than 20 days. In foster care children, AP use and use of 4 or more mental health drugs.
  - Texas State should consider investigating a root cause and consider using the data dictionary to look at regional variation, drug preferences, and prescriber types that might explain the elevated rates.

- States that had low rates on specific measures and could be consulted include:
  - ME, MO, PA and TN had fewer >20 day gaps in AP fills for children
  - CA, IL, NY, OR and WA had lower overall AP use rates
  - CA, NH, NY, and OR had lower AP use rates in children ≤5 years
  - IL, ME, OK, and OR had lower high dose rates of APs
  - AL, IL, NH, and WA had lower use rates of >2 APs
  - IL, MO, OR, and WA had lower use rates of >4 Mental Health Drugs
  - MO, PA, TN and TX had fewer >20 day gaps in AP fills for foster care children
  - CA, IL, OR and WA had lower foster care use rates of APs
  - CA, MO, OR, and WA had lower use rates of >4 Mental Health Drugs for foster care children
- The Resource Guide offers best, promising, and emerging practices as potential solutions.

AP Utilization Trends for Children Enrolled in Texas Medicaid

AP Use in Children and Adolescents aged 18 years and younger

This figure shows the rate of AP use among non-dual Medicaid clients 18 years of age and younger who paid fee-for-service in Texas compared to the 16-state mean, minimum and maximum rates[4] for 2004-2007.



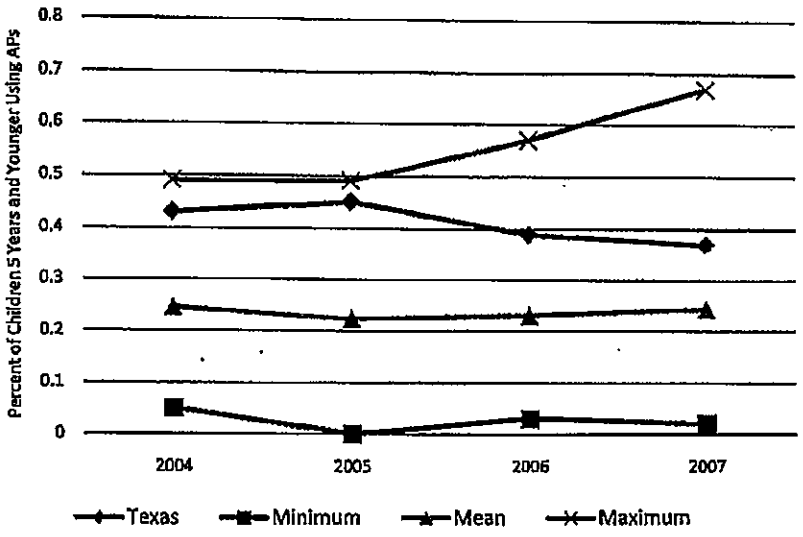
The 2007 rate represents a 16% increase from 2004.

See Data Dictionary and Resource Guide for further details on AP use in Children.

[4] Mean data points reflect the pooled average of all states included for that year. Maximum data points reflect the state with the highest rate in that year. Minimum data points reflect the state with the lowest rate in that year.

AP Use in Children Aged 5 Years and Younger

This figure shows the rate of AP use among non-dual Medicaid clients 5 years of age and younger who paid fee-for-service in Texas compared to the 16-state mean, minimum and maximum rates[4] for 2004-2007.

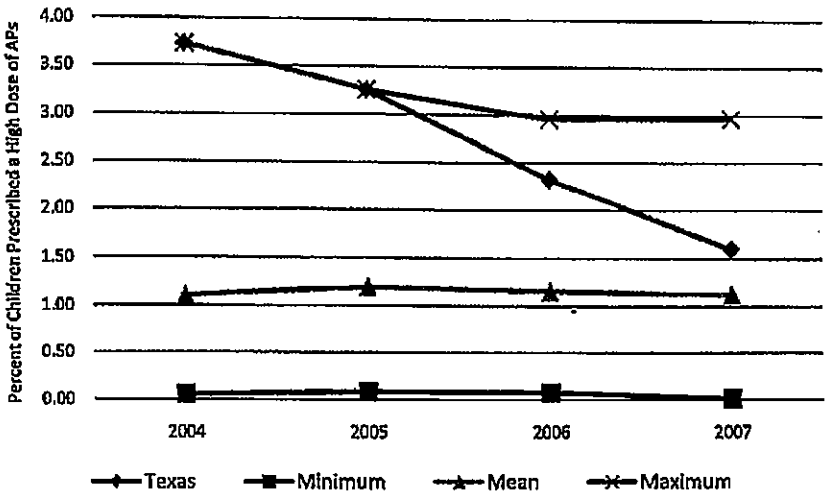


The 2007 rate represents a 14% decrease from 2004.

See Data Dictionary and Resource Guide for further details on AP use in Children.

High Dose AP Use

This figure shows the proportion of AP users (18 years old and younger) who had at least one prescription filled for a high dose AP in Texas compared to the 16-state mean, minimum and maximum rates[4] for 2004-2007. For this analysis, high dose had an age dependent definition based on the Texas guidelines[3]. Children aged 5 years and younger were defined as high dose if their dose was greater than the maximum dose defined by Texas guidelines and for those from 6 to 18 years of age, high dose was defined as exceeding twice the Texas guidelines defined maximum dose.



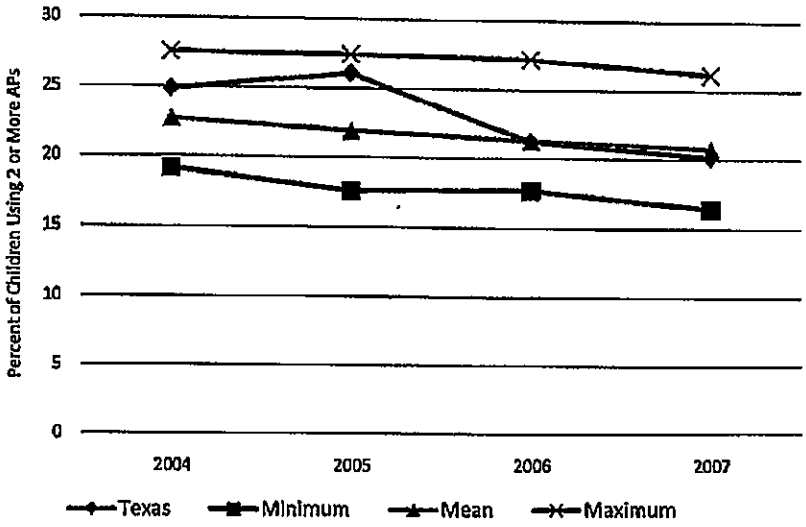
TX data partially coincide with maximum rates.

The 2007 rate represents a 57% decrease from 2004.

See Data Dictionary and Resource Guide for further details on high dose definition.

Multiple AP Use (2 or more APs)

This figure shows the proportion of AP users (18 years old and younger) who had prescriptions filled for two or more different APs in Texas compared to the 16-state mean, minimum and maximum rates[4] for 2004-2007.

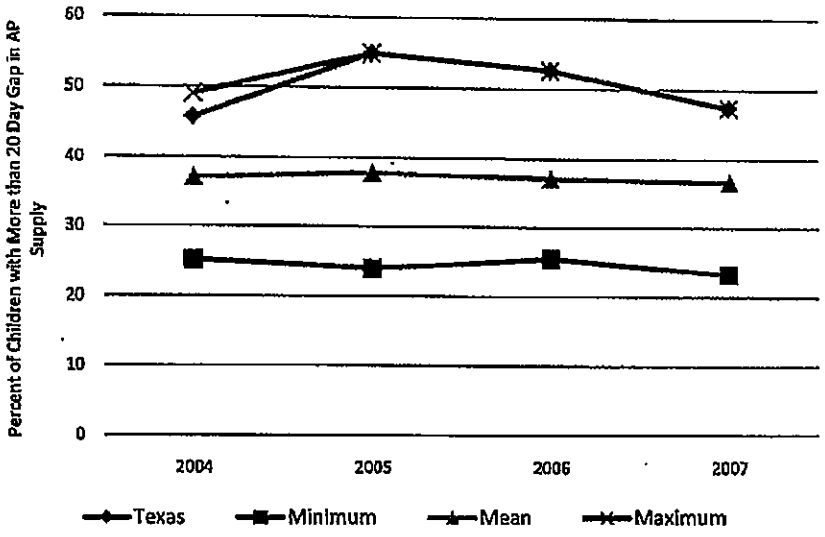


The 2007 rate represents a 19% decrease from 2004.

See Data Dictionary and Resource Guide for further details on Multiple AP use.

Gap of More than 20 Days in Filling AP Prescriptions

This figure shows the proportion of AP users (18 years of age and younger) who had a gap in AP supply of more than 20 days between AP prescription fills in Texas compared to the 15-state[5] mean, minimum and maximum rates[4] for 2004-2007.



TX data partially coincide with maximum rates.

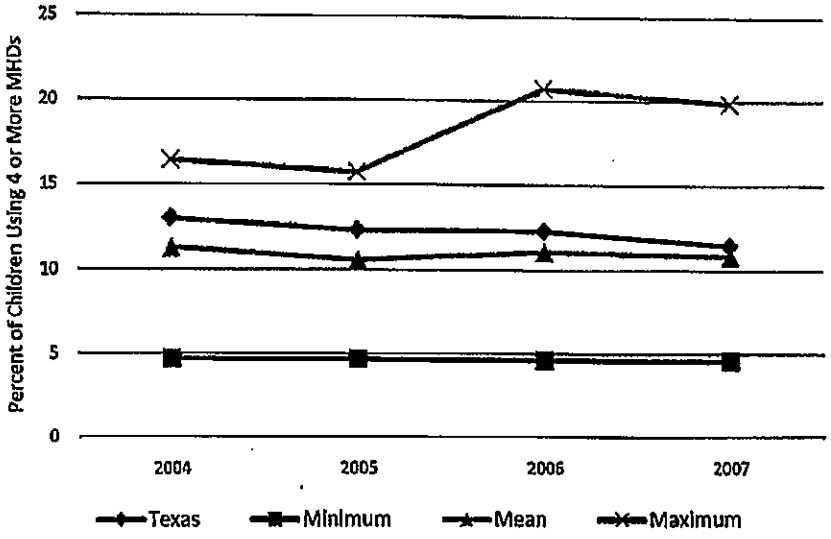
The 2007 rate represents a 4% increase from 2004.

See Data Dictionary and Resource Guide for further details on maximal gap in days.

[5] All states except Oklahoma.

Use of Multiple MHDs

This figure shows the proportion of MHD users (18 years of age and younger) who had prescriptions filled for four or more different MHDs in Texas compared to the 16-state mean, minimum, and maximum rates[4] for 2004-2007.



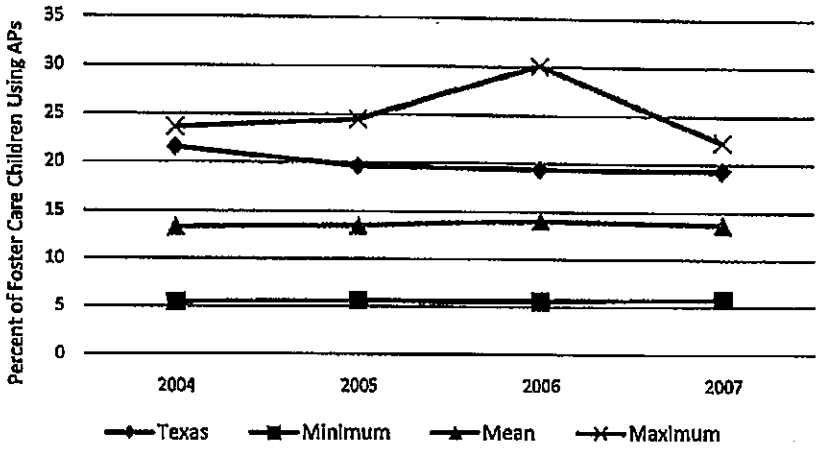
The 2007 rate represents a 12% decrease from 2004.

See Data Dictionary and Resource Guide for further details on multiple MHD use in Children.

Utilization Data and Trends for Foster Care Children Enrolled in Texas Medicaid

AP Use in Foster Care Children and Adolescents Aged 18 Years and Younger

This figure shows the rate of AP use among non-dual Medicaid clients 18 years of age and younger eligible for foster care who paid fee-for-service in Texas compared to the 13-state[6] mean, minimum, and maximum rates[4] for 2004-2007. A client is defined as being under foster care if they had at least 1 month of foster care eligibility.



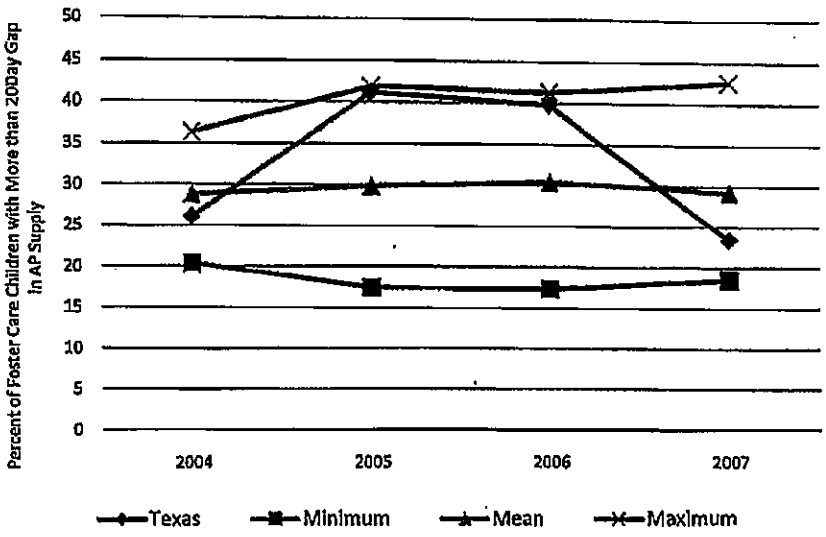
The 2007 rate represents a 10.5% decrease from 2004.

See Data Dictionary and Resource Guide for further details on AP use in Children.
See Data Dictionary and Resource Guide for further details on Foster Care Eligibility.

[6] All states except New Hampshire, New York, and Oklahoma.

Gap of More than 20 Days in Filling AP Prescriptions (Foster Care)

This figure shows the proportion of foster care AP users (18 years of age or younger) who had a gap in AP supply of more than 20 days between AP prescription fills in Texas compared to the 13-state[6] mean, minimum, and maximum rates[4] for 2004-2007. A client if defined as being under foster care if they had at least 1 month of foster care eligibility.

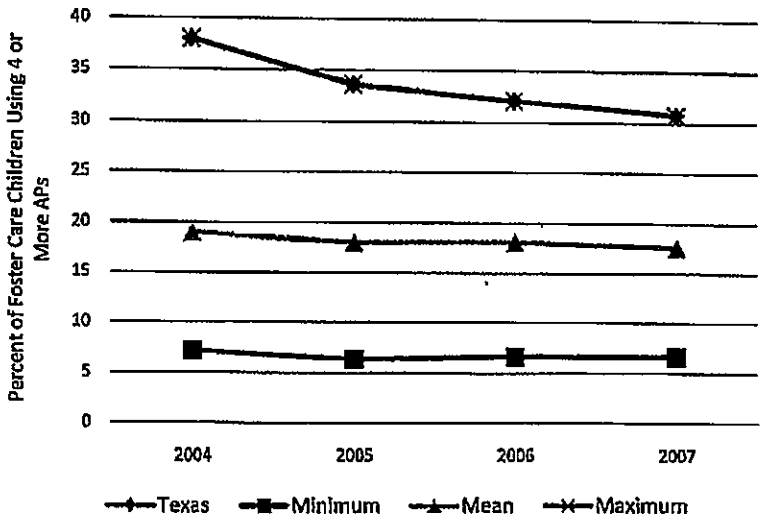


The 2007 rate represents a 10.4% decrease from 2004.

See Data Dictionary and Resource Guide for further details on maximal gap in days.
See Data Dictionary and Resource Guide for further details on Foster Care Eligibility.

Use of Multiple MHDs (Foster Care)

This figure shows the proportion of foster care MHD users (18 years of age and younger) who had prescriptions filled for four or more different MHDs in Texas compared to the 13-state[6] mean, minimum, and maximum rates[4] for 2004-2007. A client if defined as being under foster care if they had at least 1 month of foster care eligibility.



TX data coincides with the maximum rates.

The 2007 rate represents a 19% decrease from 2004.

Note: The improvement in this category is likely to be related to the release and wide distribution of the "Texas Psychotropic Mediation Utilization Parameters for Foster Children" (released in February 2005). Further improvements are being noted over the past two years with the beginning of STAR Health in April 2008 placing all Texas foster children under a single managed care provider allowing for automated tracking of all psychotropic prescriptions and consultation to prescribing physicians.

See Data Dictionary and Resource Guide for further details on multiple MHD use in Children.
See Data Dictionary and Resource Guide for further details on Foster Care Eligibility.

APPENDIX D
Medicaid Program Information

Medical Benefits for Children Enrolled in Texas Medicaid

Federal law requires that Medicaid cover a comprehensive set of benefits and services for recipients under age 21. Services that are covered for Texas Medicaid recipients under age 21 include, but are not limited to, the following:

- Physician services.
- Inpatient and outpatient hospital services.
- Laboratory and X-ray services.
- Family planning/genetics.
- Home health services.
- Physical, speech, and occupational therapy.
- Early and Periodic Screening, Diagnostic, and Treatment (EPSDT), or Texas Health Steps (THSteps) services, including periodic screening, vision, hearing, and dental services, as well as any medically necessary healthcare services.
- Behavioral health services.
- Prescription drugs.

Behavioral health services are defined as services used to treat a mental, emotional, or chemical dependency disorder. Texas Medicaid covers the following behavioral health services for enrollees under age 21:

- Care and treatment of behavioral health conditions by a primary care physician.
- Therapy by psychiatrists.
- Therapy by psychologists, licensed clinical social workers (LCSWs), licensed professional counselors (LPCs), and licensed marriage and family therapists (LMFTs).
- Inpatient care in a general acute hospital.
- Inpatient care in psychiatric hospitals.
- Outpatient adolescent chemical dependency counseling by state-licensed facilities.
- Rehabilitative and targeted case management services for individuals with severe and persistent mental illness or children with severe emotional disturbance (SED).
- Ancillary services required to diagnose or treat behavioral health conditions.
- Prescription drugs (unlimited).

Medicaid Vendor Drug Program

Texas Medicaid covers most outpatient prescription drugs through the Vendor Drug Program. The Vendor Drug Program directly contracts with over 4,100 pharmacies throughout the state to provide prescription drugs to Medicaid clients. As required by federal law, the Vendor Drug Program maintains a comprehensive formulary of all drugs of manufacturers that have signed a federal Medicaid rebate agreement.

The Medicaid Vendor Drug Program has a drug utilization review (DUR) program to ensure that prescriptions for covered outpatient drugs are appropriate, medically necessary and not likely to result in adverse medical outcomes. DUR tools include:

- Drug product enrollment
- Prospective edits at the pharmacy point-of-sale (e.g. quantity limits, alerts for drug interactions or therapeutic duplication)
- Clinical prior authorization edits
- Preferred drug list - certain drugs are preferred based on clinical efficacy, safety and cost effectiveness; non-preferred drugs require prior authorization
- Retrospective DUR interventions

Some DUR efforts relate specifically to antipsychotic medications. For instance, as part of the retrospective DUR program, between 2004 and 2010, HHSC sent eight mailings to targeted physicians to improve coordination of care for Medicaid recipients on atypical antipsychotics. Profiles of physicians' patients for which specific DUR issue(s) were identified were enclosed with the letter. One of these mailings (in February 2006) targeted doctors who prescribed to Medicaid youth in foster care.

Medicaid Health Care Delivery Models

In Texas Medicaid, most services for enrollees under age 21 are delivered through managed care. There are two managed care models in Texas Medicaid: the primary care case management (PCCM) model and the health maintenance organization (HMO) model.

Under the PCCM model, the state pays providers directly for services provided to clients. In addition, the state pays primary care providers a monthly fee of $5.00 per client for coordinating the client's care. The PCCM model operates in 202 Texas counties where the HMO model does not operate.

Under the HMO model, used in urban areas and surrounding counties, the state pays the HMO a monthly capitation fee for each client enrolled in the HMO based on an average projection of medical expenses for the typical patient. The HMO contracts with providers and pays them for services provided to their members.

There are four programs under the HMO model: STAR, STAR+PLUS, STAR Health, and NorthSTAR. The STAR program primarily serves non-disabled children, low-income families, and pregnant women residing in nine urban areas of the state. Clients have a primary care provider who serves as their medical home. The primary care provider provides preventive care, treats the majority of enrollees' conditions, and refers enrollees to specialty care when necessary.

STAR+PLUS serves aged, blind, and disabled clients, many of whom have complex medical conditions that require long-term services and supports, such as attendant care and adult day health services. These clients are assigned a service coordinator who is responsible for coordinating their acute and long-term services and supports. STAR+PLUS currently serves aged, blind, and disabled clients in 29 counties in the Bexar, Nueces, Travis, and Harris Expansion Service Areas. In 2011, it will be expanded

to serve clients in 13 counties in the Dallas and Tarrant Service Areas. Children with disabilities have the option of participating in STAR+PLUS.

STAR Health serves children in foster care and kinship care statewide. These members receive medical, dental, and behavioral health benefits through a medical home. Additional benefits include service coordination and the health passport, a web-based electronic health record.

NorthSTAR integrates the publicly-funded systems of mental health and chemical dependency services. The Department of State Health Services (DSHS) contracts with a behavioral health organization (BHO) to provide mental health and chemical dependency services to enrollees. NorthSTAR currently serves most Medicaid enrollees in the Dallas Service Area.

In addition to the health care delivery models listed above, Texas Medicaid operates a number of home and community based services waivers, including the recently established Youth Empowerment Services program (YES waiver). The YES waiver is a 1915(c) home and community-based services program that provides intensive community-based services and supports to children with severe emotional disturbance (SED) and their families, with the goals of preventing custody relinquishment and reducing or averting inpatient psychiatric hospitalization stays. In addition to regular Medicaid services, waiver participants are eligible for number of additional services as needed. The YES waiver was implemented in April 2010, in Travis County, and will be implemented in Bexar County shortly. If the waiver is determined to be cost effective in its first two years of operation, the program will be expanded to Harris and Tarrant counties.

APPENDIX E

Shortage of Child and Adolescent Psychiatrists in Texas

By Emilie A. Becker MD; Brian King, BA; Alan Shafer, PhD; Christopher R. Thomas, MD

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Abstract

This study was conducted to determine how the current shortage of Texas child and adolescent psychiatrists (CAPs) impacts the delivery of mental health care services to indigent Texas youth. First, Texas Medical Board data detailed how many counties had CAPs and how many did not. Second, statewide Medicaid data revealed the number of prescriptions for psychotropics written for Medicaid youth by CAPs and non-CAPs. Third, Local Mental Health Authority (LMHA) encounter data of youth seen by a CAP were analyzed. Fourth, state census data gave the location and characteristics of youth by county. Eighty percent of counties in Texas, predominantly rural, do not have a CAP. Non-CAPs wrote 66% of psychotropic medication prescriptions written for Medicaid youth. Those in nonmetropolitan areas were more likely to see a non-CAP than were Medicaid youth in metropolitan areas. For youth seen by an LMHA, those in rural poor counties were less likely to see a CAP than were those in urban counties. The shortage of CAPs in Texas results in an unequal distribution of psychiatric care for those receiving Medicaid prescriptions or services through LMHAs, especially in rural areas. Suggestions to correct this shortage are made.

Introduction

Texas' shortage of child and adolescent psychiatrists (CAPs) mirrors that in the rest of the country. Since the early 1980s, studies have repeatedly shown a gap between population growth and the supply of child and adolescent psychiatrists (CAPs).[1-4] Following are some of the most commonly cited reasons for this shortage:

- Fewer training programs exist, graduating fewer CAPs.[5]
- Low exposure to CAP during medical school training and delayed exposure during general psychiatry residency decreases the numbers who choose CAP.[6]
- CAP training, an extra 2 years, does not substantially increase wage-earning capacity over that of general psychiatrists.[7]
- Fewer international medical graduates are available for any specialty because of the combination of more strictly enforced immigration laws along with increased examinations.[5]
- More psychiatric residents choose careers in the newly created specialties in

geriatrics, forensics, psychosomatics, and addictions.
- Texas has an overall physician shortage.[8]

The Texas Department of State Health Services provides outpatient services throughout the state via 38 Local Mental Health Authorities (LMHAs) that cover the 254 counties in the state. The statewide safety net for the mentally ill, the LMHAs serve a widely varying number of counties, geographic areas, and populations. For example, the Texas Panhandle Mental Health Mental Retardation (MHMR) catchment area includes 21 counties that span 21,000 square miles, and their physicians saw 531 youths in 2007. Harris County MHMR (Houston) covers a single county of 2000 square miles, throughout which doctors saw 4212 youths in 2007. The LMHA in Dallas differs from the rest of the state, contracting with a managed care organization and other private providers for mental health care.

This study was a retrospective analysis of available state data to support the hypothesis that a shortage of CAPs exists and that shortage affects the care given to Texas indigent youth.

Method

Information on CAPs from the Texas Medical Board was reviewed to determine their number and current geographic locales. The US Office of Management and Budget determined the definitions of rural and urban counties used for this report (more information can be found at http://www.dshs.state.tx.us/CHS/HPRC/counties.shtm). Texas Medicaid data maintained by the Texas Health and Human Services Commission provided the number of prescriptions for Medicaid youth and the percentage written by CAPs. The LMHAs provided the number of youths seen for mental health services and the percentages seen by CAPs. State census data provided information on the location and characteristics of youth by county.

Description of data sources

Data were gathered from the following sources:

- A current list of practicing CAPs provided by the Texas Medical Board. The database comprises all medical licensure issued in the State of Texas. Texas verifies identity, age, medical school education, and examination scores. Graduate medical education and board certification are not verified, but false information can lead to disciplinary action. Physicians choose whether to list psychiatry, child and adolescent psychiatry, or pediatric psychiatry as either their first or secondary specialty.
- Psychotropic prescriptions written for Medicaid youth from the Texas Health and Human Services Commission for state fiscal year 2006.
- Children's mental health service encounters in which care is delivered by physicians at Texas LMHAs for 2007. The original data analysis included the number of service encounters according to LMHA and identification of each physician server. Each LMHA was then asked to list each physician's name by server identification; the training of each physician was subsequently verified on the Texas Medical Board Web site by the authors or by the LMHAs on the Texas Medical Board Web site. Three of the 38 LMHAs chose to do the latter. Data were obtained from all the

LMHAs.

- Census data on children and Texas come from the Population Projections for Texas developed by the Texas State Data Center at The University of Texas at San Antonio.

Results

Availability of Texas CAPs

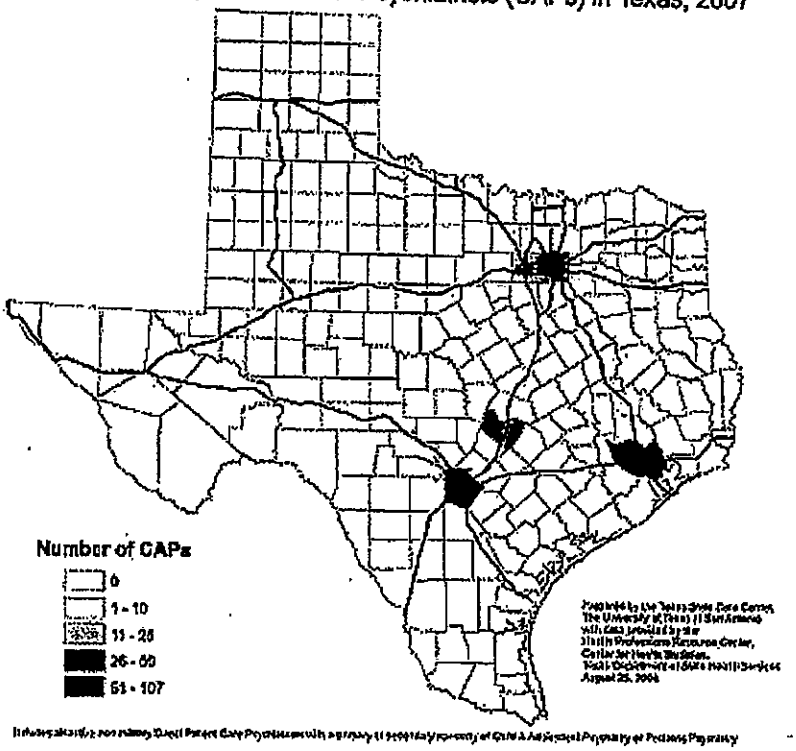
In Texas in 2007, the Texas Medical Board listed 587 licensed psychiatrists with child, adolescent, or pediatric psychiatry as a self-reported primary or secondary specialty. Of these, 408 were engaged in direct patient care (ie, neither retired, doing research/administrative work, working with the military, nor a resident or fellow). This final number is slightly inaccurate because a closer review of the findings revealed that not all of the psychiatrists who completed a 2-year child and adolescent fellowship or a pediatrics residency listed themselves as specialists in child and adolescent psychiatry. And the reverse was also true: that doctors might list themselves as specialists in CAP but not list their fellowship or board certification. But the variance appeared relatively small, accounting for less than 5% of the 408 psychiatrists. In all but one case, the psychiatrists listed their practice address rather than a mailing address.

As Figure 1 shows, of the 254 counties in Texas, 50 counties (20%) had a CAP and 204 (80%) did not. Only 3.2% of the CAPs practiced in rural counties. The map reveals that the density of CAPS correlates with urban areas and the interstate highways that connect them. In particular, many CAPs seem to work along the Interstate 35 corridor that connects Dallas-Fort Worth, Austin, and San Antonio, and the Interstate 10 highway between San Antonio and Houston.

The number of children (those younger than 19 years) in Texas was 6,730,737 in 2007.[9] Thus, Texas has 6.7 CAPs for every 100,000 children.

By sex, 248 of the 408 CAPs were men (61%), and 160 were women (39%). The racial or ethnic breakdown was 239 white (59%), 21 black (5%), 58 Hispanic (14%), 73 Asian (18%), 2 Native American/Alaskan (<1%), and 15 unknown (4%). In 2007, the Texas population from birth to age 18 years included 2,612,669 whites (38.8%), 822,056 blacks (12.2%), 3,054,219 Hispanics (45.4%), and 241,793 others (3.6%).[9]

Child, Adolescent, and Pediatric Psychiatrists (CAPs) in Texas, 2007



Psychotropic prescriptions by Texas CAPS

Texas Medicaid children and adolescents by definition are either living in poverty (based on poverty income levels) or are wards of the state. In December 2007, the children on Medicaid numbered 2,607,281 (about 38% of children in Texas).[10] In state fiscal year 2006, a total of 1,514,136 single prescriptions for psychotropics (as listed in the Drug Formulary of the Texas Department of State Health Services) were issued to 256,315 Medicaid youths younger than 18 years. Thus, 9.8% of Medicaid youth received a single prescription for a psychotropic drug. Of these prescriptions, CAPs wrote 510,995 (34%), and other specialists (eg, general psychiatrists, pediatricians, and family physicians) wrote 1,003,141 (66%). Possibly, some of the medications listed as psychotropics might have been used for medical purposes (ie, Depakote for seizures or Vistaril for skin conditions), but diagnoses were not available for analysis; however, these prescriptions appeared to be exceptions rather than the rule, and the bulk of psychotropics are prescribed by physicians other than CAPs.

The 408 practicing CAPs in Texas were matched by license number to the Texas Health and Human Services Commission Medicaid Provider ID file. Of these 408 CAPs, a subset of 336 prescribed psychotropic drugs to Medicaid children during state fiscal year 2006. These 336 CAPs prescribed an average of 1520 prescriptions (SD = 2424) to 171 Medicaid children (SD = 250), for a total of 510,995 prescriptions. In contrast, the

15,433 non-CAP Medicaid prescribers prescribed an average of 65 prescriptions (SD = 346) to 19 Medicaid children (SD = 76), for a total of 1,003,141 prescriptions.

The non-CAP Medicaid prescriber group was further examined by specialty. Eighty-two percent of prescriptions written by non-CAP Medicaid prescribers were accounted for by four self-reported primary specialties: pediatrics (32% of non-CAP prescriptions), general psychiatry (29% of non-CAP prescriptions), family practice (13% of non-CAP prescriptions), and child neurology (8% of non-CAP prescriptions).

Further analysis of the 15,433 non-CAP prescribers showed that 817 general Medicaid psychiatrists (who accounted for 29% of non-CAP prescriptions) prescribed an average of 360 prescriptions per doctor to 47 clients for a total of 294,555 prescriptions. The remaining 14,616 non-CAP, nonpsychiatrists only prescribed an average of 48 prescriptions per doctor to 17 clients for a total of 708,586 prescriptions. In sum, while as a group the nonpsychiatrists wrote most of the prescriptions for psychotropics to Texas Medicaid youth, individually each nonpsychiatrist prescribed fewer medications and saw fewer children on average than either psychiatrists or CAPs.

More CAP prescriptions were written in metropolitan counties and more non-CAP prescriptions were written in nonmetropolitan counties (chi-square(1) = 6,140, P <.001). Specifically, more prescriptions written by CAPs were observed (439,398) in metropolitan counties than were expected (422,115), and fewer were observed in nonmetropolitan counties (71,597) than were expected (88,800). For non-CAPs, fewer prescriptions were observed (811,376) in metropolitan counties than were expected (828,659), and more were observed in nonmetropolitan counties (191,765) than were expected (174,482).

Service encounters by Texas CAPs

In 2007, the 38 LMHAs reported 103,034 physician service encounters for child mental health service. Of these, 77,034 (75%) service encounters were delivered by a CAP. The rest were seen by non-CAPs, most of whom were adult psychiatrists.

Of the 51,764 physician service encounters at 10 urban LMHAs, a total of 42,615 (82%) were delivered by CAPs. In contrast, of the 51,270 physician service encounters at 28 rural LMHAs, only 34,419 (67%) account for care delivered by CAPs, a statistically significant difference (chi-square(1) = 3,151, P <.001).

Subsequently, LMHAs were classified also according to the average per capita personal income for their catchment counties by using a median split. Half of the LMHAs served counties where the average per capita income was greater than $30,137; these were categorized as high per capita income LMHAs, and the other half were classified as low per capita income LMHAs. At 56,650 (82%) of the 68,605 physician service encounters at high per capita income LMHAs, the care was delivered by CAPs. In contrast, of the 34,429 physician service encounters at low per capita income LMHAs, only 20,474 (60%) involved care delivered by CAPs, a statistically significant difference (chi-square(1) = 6,414, P <.001).

Finally, LMHAs were categorized according to the percentage of their catchment population that was Hispanic or Black or both. A median split was used to classify LMHAs serving a low minority population versus a high minority population. Half the LMHAs served counties where the minority population was less than 37%; they were categorized as low minority population LMHAs, and the other half were categorized as

high minority population LMHAs. At 25,761 (72%) of the 35,694 physician service encounters at low minority LMHAs, the care was delivered by CAPs. Similarly, of the 67,340 physician service encounters at high minority population LMHAs, the care was delivered by CAPs in 51,273 (76%). This statistically significant difference (chi-square(1) = 194, $P < .001$) appears to be related to the distribution of minorities, who are disproportionately located in urban areas. Minorities in rural areas had the same lower percentage chance of seeing a CAP as did their nonminority peers.

Discussion

Studies have estimated that 14.38 CAPs per 100,000 youth are needed under a managed care system.[11] The ratio of CAPs per 100,000 varies widely, ranging from 1.3 in West Virginia to 17.5 in Massachusetts.[12] With 6.7 CAPs per 100,000, Texas has somewhat less than half the recommended number estimated to meet the mental health needs of its population. Most of these CAPs are concentrated in urban areas. While most of the Texas LMHAs have been able to employ CAPs in providing child mental health services, access to CAPs still differs significantly, with urban and higher per capita counties faring better than rural or impoverished counties. Some of the rural LMHAs have started to use telepsychiatry, which might explain some of the findings of utilization of CAPs in LMHAs with few or no local CAPs.

Minorities are disproportionately underrepresented in the number of child psychiatrists.[13] Given that Hispanic teens are now the majority in Texas, the small number of Hispanic psychiatrists is particularly striking. The 2001 Surgeon General's report found that although mental disorders are prevalent within minority populations in the United States, minorities are less likely to seek care, and the care they do receive is often of a lower quality than care provided to nonminorities.[14] Having more minority psychiatrists would help destigmatize mental illness for minorities and improve that barrier to accessing care.

In general, Texas Medicaid children and adolescents appear to frequently get at least a single prescription for a psychotropic drug from either a primary care doctor or a general psychiatrist. However, when the emotional problems become more severe, these patients seem to receive specialty help, as reflected by the increased number of prescriptions per patient by a CAP.

Few would disagree that the number of CAPs needs to match the population growth in Texas. How to best address this issue, however, creates much debate. The supply of CAPs is primarily determined by recruitment into training, number of training positions, and retention of graduates in practice. The following are some suggestions to consider:

- Increase the number of medical students.
- Increase recruitment into child and adolescent psychiatry.
- Increase funding for the number of training positions in CAP.
- Waive the debt faced by graduating CAPs through loan-forgiveness programs.
- Study CAP access to show it improves patient outcome and reduces overall health care costs.
- Place CAP fellows in rural areas for periods of their training.
- Increase psychiatric reimbursement rates for child and adolescent patients.

- Streamline psychiatric training to reduce the total number of years required to become a CAP.

Given that the number of CAPs is unlikely to increase to sufficient numbers, additional suggestions to maximize access are to use telepsychiatry to deliver care by urban CAPs. Advanced practice registered nurses and physician assistants with training in child and adolescent mental health can also fill the unmet need. Lastly, integrating CAPs into pediatric and primary care clinics leverages CAP access. Meanwhile, Texas suffers from a shortage of CAPs. Changes are needed to improve treatment for the vulnerable population of the young mentally ill.

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Appendix F

STAR Health (Texas Foster Care)
Psychotropic Medication Utilization Review
Frequently Asked Questions

What is a Psychotropic Medication Utilization Review?
STAR Health, the Foster Care managed care program administered by Superior HealthPlan Network and Integrated Mental Health Services, conducts a review for children in foster care who receive medications for mental or behavioral health conditions to ensure the medication practices are in compliance with the "Psychotropic Medication Utilization Parameters for Foster Children" (the Parameters) as developed by the Texas Department of State Health Services (DSHS).

How are members referred for screenings and reviews?
There are several ways that a member may receive a screening and then a review

- STAR Health routinely monitors the medications prescribed through data transfers from the State and through our ongoing service management for members, and
- Referrals for a review can be made by any caseworker, judge, foster parent, medical consenter or other concerned entity.

What does this review involve?
The review process begins with a screening to ensure that any child receiving psychotropic medication:

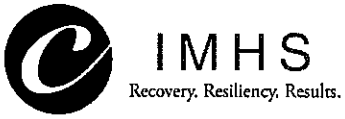
- Has received a thorough assessment including a diagnosis of a psychiatric condition
- Is not receiving five or more psychotropic medications at the same time
- Is not receiving multiple medications for the same condition(s) as described in the parameters
- Is not receiving polypharmacy for a condition without a trial on a single medication
- Is not receiving medication dosages exceeding manufacturers recommendations
- Is receiving appropriate medications if of a very young age
- Is receiving medication consistent with the stated diagnosis; and
- Ensuring that primary care physicians are consulting with a psychiatrist when treating conditions other than Attention Deficit Hyperactive Disorder (ADHD), uncomplicated Anxiety Disorders or uncomplicated Depression.

Who conducts this screening?
The clinical staff (nurses and licensed behavioral health professionals) at Integrated Mental Health Services (IMHS), the contracted behavioral health management vendor for STAR Health, is responsible for conducting these screenings.

What do I do if I (the prescriber) receive a request for information during the screening process?
Requests for information to the STAR Health contracted prescriber by clinical staff do not require a separate release of information. Both the Department of Family and Protective Services (DFPS) and DSHS support the Psychotropic Medication Review process, and ask for your participation.

What do I do if the DFPS Residential Child Care Operation receives a request for information during the Psychotropic Medication Utilization Review process?

The Residential Child Care Operation may release to STAR Health: Physician notes, treatment/service plans medication logs and psychological evaluations, after the operation receives



a request from an identified representative of STAR Health that specifies information needed for the purpose of Psychotropic Medication Utilization Review.

If STAR Health requests additional documents, then the Residential Child Care Operation must obtain additional written consent of the DFPS Child Protective Services caseworker.

What happens when the screening finds that one of the conditions above is not met?

When the screening indicates that a foster child's medication regimen falls outside the Parameters, STAR Health gathers any additional information needed from the prescriber, the residential child care operation, DFPS caseworker, medical consenter or others. The case then is referred to the STAR Health Medical Director to determine the need for a formal review. Please be aware that triggering of a medication review based on the Parameters is not viewed as a complaint against a provider.

How is the review conducted?

During this review, the Medical Directors or other qualified child psychiatrist or pediatrician will contact the prescriber to obtain more detailed information about the child's current diagnoses, medication regimen, and rationale for treatment. The prescriber's participation in the review is expected, and a separate release of information is not required. This discussion between the STAR Health physician and the prescriber is an opportunity to confer about the case and identify where prescribing is not meeting the Parameters. If the prescribing falls outside the parameters, the physician will compare prescribing to the STAR Health approved Clinical Practice Guidelines or community standard.

Must I change my prescribing of medications to foster children because of the review?

The prescriber will never be told to change medications during a Psychotropic Medication Utilization Review. STAR Health realizes that many physicians may have just begun to see a foster child, or the child may have come to them on multiple medications. During the Psychotropic Medication Utilization Review, a psychiatrist may call and discuss the child's medication history, symptom status, and response to treatment. In some instances, opportunities to reduce polypharmacy and/or to reduce side effects may be identified. Our goal is to improve the care for foster children in the State of Texas.

What happens to the information after the review?

If a psychiatrist conducts a review, the results (including recommendations) will be written and included in the member's record at STAR Health. Copies of the results will be sent to any referring entity and will be available to caseworkers and/or medical consenters at their request. The Psychotropic Medication Utilization Review findings are documented and cases may be referred to the DFPS Medical Director for further review.

How do I make a referral?

Referrals can be made by calling STAR Health Member Services 1-866-912-6283.

APPENDIX G

List of Acronyms

AACAP – American Academy of Child and Adolescent Psychiatry
ADHD – Attention deficit/hyperactivity disorder
ARI - aripiprazole
BMI – Basal metabolic index
BP – bipolar disorder
CLZ – clozapine
DFPS – Department of Family and Protective Services
DSHS – Department of State Health Services
ECG - electrocardiogram
EPS – Extrapyramidal symptoms (neuromotor adverse effects, including muscle cramping, involuntary movements, extreme restlessness, and a syndrome similar to Parkinson's disease with muscle rigidity)
FDA – U.S. Food and Drug Administration
FGA – First generation antipsychotic
HAL - haloperidol
HHSC – Health and Human Services Commission
ILO - iloperidone
MOL - molindone
NIH – National Institutes of Health
NIMH – National Institute of Mental Health
NMS - Neuroleptic Malignant Syndrome
OCD – Obsessive compulsive disorder
ODD - Oppositional defiant disorder
OLZ - olanzapine
POL – Prospective open label study
PAL – paliperidone
PDD – pervasive developmental disorders, also known as autism spectrum disorders
PER - perphenazine
PTSD – Post-traumatic stress disorder
QTP - quetiapine
RCT – Randomized double-blinded placebo-controlled study
RIS - risperidone
SGA – Second generation antipsychotic
TD - Tardive dyskinesia (a movement disorder)
T-MAY – Treatment of Maladaptive Aggression in Youth
TRAAY – Treatment Recommendations for the Use of Antipsychotics for Aggressive Youth
ZIP - ziprasidone

APPENDIX H

Antipsychotic Medication Use in Medicaid Children and Adolescents: Report and Resource Guide From a 16-State Study

Medicaid Medical Directors Team with Rutgers to Develop a Resource Guide to Better Care

Introduction

Increased use of atypical antipsychotic medications for a broadened range of patients and indications, often off-label, has raised a range of policy challenges for payers, patients and clinicians.[1] These challenges occur in the context of widespread need for mental health services for children and adolescents, who face a variety of barriers to mental health evaluation, psychosocial treatment and other mental health services.[2,3] In response to these concerns, the challenges of mental health services in Medicaid were discussed among State Medicaid Medical Directors and investigators from the Rutgers CERT (Center for Education and Research on Mental Health Therapeutics) in June 2007 during an Agency for Healthcare Research and Quality (AHRQ) supported Medicaid Medical Directors Learning Network meeting. Out of that discussion, State Medicaid Medical Directors and the Rutgers CERT developed a plan for a collaborative project to examine the use of antipsychotic (AP) medications for children and adolescents in Medicaid. Shared measures and a data dictionary were developed and used as a guide by Sates to conduct analyses of their own data for this project. Vital convening, expertise, and other support for the project was provided through the AHRQ-funded Rutgers CERT and Medicaid Medical Directors Learning Network (MMDLN).

The National Association of Medicaid Directors and the National Association of State Mental Health Program Directors provided additional review and input. Ultimately, a consortium of 16 States collaborated on the project with the Rutgers CERT, representing a combined enrollment of 12 million children and adolescents in Medicaid. The purpose of the collaborative was to:

- Conduct exploratory analyses in each State on antipsychotic medication use rates and trends for children and adolescents in fee-for-service Medicaid;
- Develop a set of preliminary safety, quality, or appropriate-use indicators to support analysis and monitoring of treatment patterns;
- Identify State-specific programs and policies related to improving the use of antipsychotic medications;
- Provide a forum for discussion of policies and programs for optimizing AP medication prescribing among States; and
- Develop a compendium of State practices that could be shared with other States to address issues related to AP use in children and adolescents.

Q&A What Tools and Resources are in the Report and Resource Guide?

1. A detailed description of how 16 States produced AP and Mental Health Drug utilization data using their pharmacy claims systems.

2. A data dictionary and methodology that can be adapted by States to develop similar analyses/reports.

3. An overview of the utilization of AP medications from pooled results of analyses in the pediatric fee-for-service Medicaid population of 16 States.

4. A compendium of State-provided information from the States on a total of 36 practices related to AP utilization issues, categorized by the contributing States as mature, promising or emerging based on collaboratively-developed definitions.

Which Stakeholders May Find the Resource Guide Helpful?

State Medicaid, Mental Health, and Child Welfare Agencies: Commissioners, Medical Directors, Pharmacy Directors, program staff, Quality Assurance staff, and others interested in AP medication utilization controls and quality improvement in Medicaid.

State Leaders: Governors, legislators, and their staff who provide leadership on health policy and/or budget.

Clinicians and Provider Organizations: Physicians, pharmacists, nurse-practitioners, other mental health professionals; Medicaid managed care organizations, mental health clinics, and other provider organizations who treat children and adolescents with mental health disorders.

Other Nongovernmental Health Care Leaders at State and Local Levels: Members of community organizations, consumer groups, professional societies, provider associations, quality improvement associations, business coalitions, policy analysts, and others who want to stimulate action on health care quality improvement.

Q&A What Measures Were Developed as Flags to Assist States in Measures of Program Performance?

To support exploratory analyses of AP medication use for children and adolescents in the 16 Medicaid States, the project participants consensually identified five preliminary core measures of AP medication and total Mental Health Drug (MHD) utilization that served to flag potential quality and safety issues. They include:

- Use of AP medications in children 5 years and younger;
- Use of high doses of AP medications;
- Use of multiple AP medications any time during a calendar year (including both concurrent and non-concurrent use);
- Maximal gap in days between AP medication claims as a potential marker of adherence; and
- Use of multiple MHDs any time during a calendar year (including both concurrent and non-concurrent use).

What Were Selected Findings from the 16-State Project?

- In 2007, pooled results of State analyses indicate that a total of 193,178 children or adolescents received an AP prescription, representing 1.6 percent of the total FFS population under 19 years of age. This rate represents about a 10 percent relative increase over the comparable rate in 2004 of 1.45 percent.
- Children in foster care (12.4 percent) were prescribed AP medications at much higher rates than those not in foster care (1.4 percent).
- Pharmacy claims data can be used to explore utilization of AP medications and mental health drugs across multiple State Medicaid programs.
- Preliminary metrics utilized in exploratory analyses can serve as useful flags in framing a discussion around quality and safety related to AP use.
- States varied in terms of the populations covered, organizational structure, mental health contracts, statutes and codes.
- These efforts represent important first steps in a collaborative effort with considerable potential for public health impact in improving pediatric mental health treatment and outcomes in the vulnerable populations served by the Medicaid programs.

Q&A What Was Learned by Collaborators in the Project?

This project provided an opportunity for States to come together to discuss their experience with policies and practices related to the challenging issue of prescribing AP medication to children and adolescents, and a framework for identifying issues in their AP utilization trends. It also helped participating States make more effective use of their own data to monitor and address issues of AP medication prescribing by providing a collaboratively agreed upon set of core measures and a standardized approach to data collection and analysis. Further work is planned to develop measures that address concurrent use of multiple medications, within and between class; use of APs across diagnostic subgroups; care processes for evaluation, monitoring, and psychosocial treatments; measurement of treatment adherence; and other aspects of treatment that can be used within and across States to improve measurement, monitoring and management of medication utilization patterns. Participation in the Project helped participating States to assess treatment patterns and policies in their State, to become more aware of promising practices in other States, and to develop and extend initial initiatives to address quality concerns and encourage use of evidence based practices. Most importantly, this project demonstrated the value of working collaboratively to measure and monitor treatment practices more broadly for the children and adolescents of the United States who suffer from a psychiatric disorder. Ultimately, the objective of this project is to foster more collaboration and information sharing among the States to identify and develop best practices that provide America's children and adolescents with the right care at the right time for the right reasons.

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ANTIPSYCHOTIC MEDICATION USE IN MEDICAID CHILDREN AND ADOLESCENTS: Report and Resource Guide From a 16-State Study

This report is the product of a collaboration of 16 States, the Medicaid Medical Directors Learning Network (MMDLN) and the Rutgers CERTs (Center for Education and Research on Mental Health Therapeutics).

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Foreword

The *Report and Resource Guide* on improving quality in the management of antipsychotic use among Medicaid children, and its accompanying data dictionary and compendium of State practices, were motivated principally by the desire of the consortium to provide information that would be useful for State officials, across the nation, in their efforts to improve quality of mental health care for their Medicaid populations. We hope that they will also be useful to others who are concerned with these aims. Incorporating pooled results from States' analyses of their antipsychotic and mental health drug use derived from claims data, the *Report and Resource Guide* aims to provide information that can contribute to State efforts to assess the quality of care in their programs, across counties and prescribers, using quality improvement strategies best suited to State conditions. The States mentioned in this guide gave permission to use their data for illustrative and comparative purposes so that others could learn by their examples.

The *Guide* and compendium of practices were developed with the goal of contributing to the efforts of State leaders who struggle with quality improvement and facilitating the sharing of expertise, ideas, knowledge, and solutions. The various sections may be of particular interest to different users. For example, Sections 1, 4, and 6 may be most useful to senior leaders who are responsible for making the case for mental health quality improvement and taking action, while Sections 2, 3, and 5 may be most useful to program staff involved in developing and implementing specific quality improvement strategies. The goal, of course, is that all groups work on these topics as a team. It is within those discussions and sharing and working together we hope to achieve what we set out to do—help States improve the quality of mental health care and prescription drug use.

Many people for whom these learning tools were intended—State elected and appointed leaders as well as officials in State health departments, mental health and children's programs, Medicaid offices, and other Medicaid officials and stakeholders—provided comments and feedback throughout the development and finalization process. We offer our thanks to all the contributors for this input, and hope that they will use the *Report and Resource Guide,* State practices, and data dictionary in many different ways: to assess their current structure and status, to create new quality improvement programs, to build upon existing programs, and to share with their partners including consumer groups; managed care organizations; mental health clinics; and the clinicians who care for the often-vulnerable population of Medicaid beneficiaries. If you have any comments or questions on the *Report and Resource Guide*, please contact:

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INTRODUCTION

By one estimate, more than 15 million children and adolescents in the United States have a diagnosable psychiatric disorder, often leading to functional impairment and developmental delays in academic, emotional, social, and/or behavioral skills.[1] Many children and adolescents with mental health needs face a variety of barriers to mental health evaluation, psychosocial treatment and other mental health services.[2] At the same time researchers and payers have noted increased and broadened use of antipsychotic medications for a wide range of clinical indications in children, raising a range of policy challenges for Medicaid programs and other payers, patients and clinicians.[3] In response to these concerns, the challenges of mental health services in Medicaid were discussed among State Medicaid Medical Directors and investigators from the Rutgers Center for Education and Research on Mental Health Therapeutics (CERTs) in June 2007 during an Agency for Healthcare Research and Quality (AHRQ) supported Medicaid Medical Directors Learning Network meeting. Out of that discussion, State Medicaid Medical Directors and the Rutgers CERTs developed a plan for a collaborative project to examine the use of antipsychotic (AP) medications for children and adolescents in Medicaid. States provided the analysis of data and policies reported in this guide. Vital convening, expertise, and other support for the project was provided through the AHRQ-funded Rutgers CERTs and Medicaid Medical Directors Learning Network (MMDLN). The National Association of Medicaid Directors and the National Association of State Mental Health Program Directors provided additional review and input. Ultimately, a consortium of 16 States participated, representing a combined enrollment of 12 million children and adolescents in Medicaid. The purpose of the collaborative was to:

- Conduct exploratory analyses in each State on antipsychotic medication use rates and trends for children and adolescents in fee-for-service Medicaid using a comparable set of indicators that could "flag" possible safety and quality issues;
- Provide a forum for discussion of policies and programs for optimizing AP medication prescribing among States; and
- Develop a compendium of State practices classified by the contributing States as mature, promising and emerging according to a consensually developed classification matrix created for this project by the project participants that could be shared with other States to address AP utilization issues.

Report and Resource Guide

The *Report and Resource Guide* provides a set of sections that provide information on aspects of utilization from pooled data, relevant State policies, and definitions for States to use claims data in addressing issues regarding antipsychotic medication prescribing for children and adolescents. Each State's environment and Medicaid program faces differing pressures, needs, and opportunities. The *Guide* provides information on the 16-State collaborative effort that can inform efforts to examine and understand antipsychotic use and trends related to claims data and utilization flags in each State, including the consortium's development of a common set of potential safety and quality measures for exploratory analysis of antipsychotic medication utilization. This initial set of measures, developed based on feasibility of calculation by State data analysts under the project's time and resource constraints, provided a framework for initial

exploration of use patterns and aims to provide the starting point for a more fully developed set of metrics for monitoring treatment patterns over time and across subpopulations, geographic areas and providers. The *Guide* also provides information on State practices related to quality improvement that may inform future activities. These materials are compiled with the aim of assisting efforts to foster prescribing patterns that are supported by evidence, and with the objective of maximizing optimal treatment and health outcomes for the child and adolescent Medicaid population.

The work of the Antipsychotics in Children consortium, which underlies this report, reflects a unique collaboration of State leaders and researchers. Noteworthy was the active involvement of State officials from both Medicaid and Mental Health agencies. Both sets of expertise were key in the project's efforts to address the complex programmatic and clinical issues that influence the care of children and adolescents with mental health conditions. Perhaps more importantly, we all learned from each other and developed a deeper appreciation of the complexities of these issues, as well as the importance of collaboration between Medicaid and mental health programs and between States.

What Tools and Resources are in the Report and Resource Guide?

- A detailed description of how 16 States produced AP and mental health drug utilization data using their pharmacy claims systems.
- A data dictionary and methodology that can be adapted by States to develop similar analyses/reports.
- An overview of the utilization of AP medications in the pooled pediatric FFS Medicaid population of 16 States.
- A description of programs and policies regarding AP medication utilization controls for each of the 16 States.
- A compendium of State-provided information from the States on a total of 36 practices related to AP utilization issues, categorized by the contributing States as mature, promising or emerging based on collaboratively-developed definitions.

What is the Medicaid Medical Directors Learning Network?

The Medicaid Medical Directors Learning Network (MMDLN) was designed to assist clinical leaders in identifying and applying the latest research findings and related information to address high-priority policy and program issues, especially related to quality assurance, quality improvement, and coverage decisions. The current group, composed of State Medicaid Medical Directors from 42 States, began its work in November 2005. The network enables Medicaid Medical Directors to:

- Exchange ideas with their peers and foster a community that encourages colleagues to gather ideas and share experiences with one another;
- Gain access to resources, such as studies, reports, and decision-support tools developed by State Medicaid agencies, AHRQ, and other sources; and
- Foster collaboration to solve problems by working together on issues related to advancing the health of Medicaid enrollees.

Which Stakeholders May Find the Report and Resource Guide Helpful?

- **State Medicaid, Mental Health, and Child Welfare Agencies**: Commissioners, medical directors, pharmacy directors, program staff, quality assurance staff, and others interested in AP medication utilization controls and quality improvement for children and adolescents in Medicaid.
- **State Leaders**: Governors, legislators, and their staff who provide leadership on health policy and/or budget.
- **Clinicians and Provider Organizations**: Physicians, pharmacists, nurse-practitioners, other mental health professionals; Medicaid managed care organizations, mental health clinics, and other provider organizations that deliver care for children and adolescents.
- **Other Nongovernmental Health Care Leaders at State and Local Levels**: Members of professional societies, provider associations, quality improvement associations, voluntary health organizations, business coalitions, community organizations, consumer groups, research analysts, and others who want to stimulate action on health care quality improvement at the State level.

What is the Structure and Organization of the Report and Resource Guide?

The *Report and Resource Guide* is divided into sections that can be read separately to assist the reader in easily finding specific and relevant information so that one can understand the measures and trends and be able to reproduce similar utilization numbers and rates using definitions and templates. The sections are organized as follows:

Section 1: Background—Provides background on issues in use of antipsychotic medications in children and adolescents as context for the issues of "too many, too much, too young" identified by the Medicaid Medical Directors.

Section 2: Methods and Project Timeline—Discusses methods and processes so that a State can assess the resources and timelines needed to analyze their own data and practices.

Section 3: Data—Describes the pooled estimates from State analyses of antipsychotic utilization among fee-for-service (FFS) Medicaid youth in 16 States.

Section 4: Interventions/State Practices—Discusses State-specific practices related to antipsychotic treatment, classified by the States as mature, promising, or emerging.

Section 5: Change Management—Discusses system strategies for improving quality, employing a systematic approach for using data to collaborate with local mental health leaders, contractors and prescribers.

Section 6: Lessons Learned— Describes how States can work together going forward to address quality and safety issues in children, adolescents and adults using antipsychotics and other mental health medications.

Epilogue: Consequences of Participation— Describes the impact and consequences of State participation in the project, based on follow-up interviews conducted in September and October of 2009.

State Practices Attachment: Provides State-supplied descriptions of practices designed to address issues of AP medication prescribing. Each State's practices are presented using a standard format with standard information elements detailing 36 mature, promising, and emerging practices.

Data Dictionary: Data dictionary used to provide a common framework for the States' analyses of rates and trends of AP and mental health medication use utilizing their claims files. It includes a tool to facilitate comparison of State-specific features to those of the 16 States in this project.

Blank Excel Spreadsheets: Provides a set of blank downloadable Excel spreadsheets to recreate the various data tables.

National Drug Codes: An Excel workbook providing the National Drug Codes used for this project.

Challenges

It is important to note that during the planning process many measures were proposed and considered. The measures utilized were selected based on feasibility of implementation by State data analysts under the substantial constraints of resources and time available for this project, which limited the complexity of measures that could be calculated. To test these differing measures, Washington State computed the measures using their data, and other States tested whether their claims systems had a similar capacity. After several months of testing, the project participants arrived at a set of five core measures (age, AP dose, two poly-pharmacy measures, and gaps in prescriptions) based foremost on feasibility of capturing the measures from the majority of the participating State claims systems, given the constraints of time and data analysis resources under which this exploratory project operated. The validity of the measures was secondary. For example, as an exploratory measure of poly-pharmacy that could be easily computed by States, we examined use of multiple medications over a calendar year, rather than undertaking the more complex analyses that would be required to estimate concurrent use of multiple medications at a point in time, which is an aim of the collaborators for a subsequent stage of work. Similarly, the "gaps in adherence" measure represents an exploratory analysis that is a first step toward more sophisticated measurement of adherence to medication regimen, which will be of increased importance as work is extended to the population of Medicaid adults with chronic mental illnesses. For high AP dosing, age, and use of multiple APs and MHDs, we chose the Texas Foster Care standards, which are a set of consensus standards developed by the State of Texas to guide practice in this area. Also, while information from States is reviewed in a parallel fashion throughout the *Guide*, definitive comparisons and generalizations among States cannot be made because a variety of local factors, such as population mix, statutes, rules, and secular trends that influence utilization numbers. Perhaps more importantly, analyses were

conducted in parallel by individual States using separately developed statistical programs and coding.

While this distributed model made for less ability to conduct statistical analysis and adjust for differences in the State populations, it allowed more States to participate in this exploratory work by reducing the time that would likely have otherwise been required to implement data sharing agreements. While the data dictionary provided definitions for the measures, and a common set of indicators, it should be noted that variations in details of inclusion criteria, mix of eligibility categories, differences in diagnostic profiles and clinical characteristics, and other cross-State variations limit the inferences that can be drawn from the raw State-to-State differences in our analyses. These were not adjusted for differences in diagnostic and other characteristics of the State populations as is planned for future analyses. For example, the clinical makeup of the population of children and adolescents receiving FFS Medicaid (on which the States' analyses focused) varies from State to State. There are variations in managed care enrollment and procedures across States that influence the composition of the child and adolescent FFS Medicaid population, which includes higher concentrations of children with disabilities, foster care children, and other subgroups at higher risk of mental health problems in some States than in others. There are also a variety of program and policy differences that affect comparability.

It is also important to note that the utilization indicators used in this project as flags for potential safety concerns were developed by consensus of the project participants. The indicators would need to be vetted more broadly and their relationship to patient outcomes studied if widespread adoption were desired. In future work, the consortium aims to develop and implement measures that, while more complex to calculate, provide improved measurement of such key constructs as adherence and poly-pharmacy.

Nevertheless, the analyses conducted by each State provided an important step forward. Examination of patterns across and within States represents a first and critical step in understanding observed variations. Further analysis can seek to understand the parameters that underlie the variation, whether related to geography, policy, access to care or provider/population characteristics, and most importantly, which of these variations are associated with better or worse outcomes.

Describing State-specific interventions promotes understanding of how to monitor and manage pharmacy policy and how to work with community partners. Interventions ranging from the "hard edit" (the categorical denial of a prescription fill that falls outside approved parameters) to education and consultation are described in the *Guide,* as well as approaches ranging from stakeholder engagement to State statutes affecting AP use. All these activities are shared in the spirit of transparency and learning with the acknowledgment that their ultimate value remains to be determined, based on locally achieved evidence of outcomes and peer-reviewed publications describing practices and processes.

SECTION 1
Background

Determining the most appropriate approaches to management of AP medication use in children and adolescents is an important and challenging area for both practice and policy. In determining benefits for children and adolescents covered under Medicaid, State Medicaid programs can play a role in shaping clinician and pediatric use of AP medications. In this *Guide,* "AP medications" refers to the following:

- First generation antipsychotic (FGA) medications such as chlorpromazine (Thorazine), haloperidol (Haldol), and perphenazine (Trilafon).
- Second generation antipsychotic (SGA) medications such as risperidone (Risperdal), olanzapine (Zyprexa), and aripiprazole (Abilify).
- In addition, the term "mental health drugs" (MHD) is used to refer to a broader list of psychoactive prescription medications that include the AP medications as well as antidepressants, anxiolytic/hypnotics, mood stabilizers, sedatives, and other drugs used to treat attention-deficit disorder, anxiety, sleep disorders, and other mental health problems.
- The Food and Drug Administration (FDA) approves medications for specific indications. Practitioners may still prescribe FDA-approved medications for other indications—a practice referred to as "off-label" use, which may or may not be supported by clinical evidence. FDA approvals of psychoactive and other medications with indications for children and adolescents under age 18 have changed and will continue to change over time.

Clinical Concerns

Concerns among state staff and other collaborators about the current use of AP medications in children and adolescents included among others:

- The possibility that some children may receive care that is largely limited to medications without receiving adequately comprehensive mental health evaluations and other mental health services appropriate to their needs.
- Concerns about the application of diagnostic criteria for bipolar illness and its impact on antipsychotic use in children and adolescents.
- Aspects of utilization patterns including multiple psychotropic medication prescribing, within and between drug classes; utilization of appropriate dosages; and utilization in very young children, such as those under age 6.
- Relatively high rates of off-label use (particularly in younger children and in other subgroups of special concern such as foster care youth), considering the limited knowledge that is available about long-term effects of AP medications on the developing nervous system.
- Strategies to reduce risks related to the weight gain and metabolic effects associated with SGA medications.

Access to Services

By one estimate, up to 15 percent of children and adolescents under age 18 who have emotional, behavioral, or mental disorders also suffer functional impairment.[1] Only one in five of these children and adolescents receive services from an appropriately trained professional.[4] Access to treatment is limited, especially in the public mental health systems, largely due to a shortage of child and adolescent psychiatrists.[2]

Application of Diagnostic Criteria

Beginning in the 1990s, the use of bipolar (BP) illness as a diagnosis evolved rapidly in child psychiatry and primary care. Current efforts seek to distinguish the small number of children whose symptoms closely fit the Diagnostic and Statistical Manual (DSM) criteria for BP from the larger number who have received the diagnosis of BP, but whose behaviors do not closely fit DSM criteria.[5] The proposed draft DSM-5 recommendations include a new term, "temper dysregulation disorder" which addresses the issue of mood swings and irritability, and perhaps more accurately describes the chronic nature (greater than 12 months) of excessive temper, over-reactions to stress, and the frequency and nature of mood swings in the child than the current DSM-4 criteria. It has yet to be seen if these recommendations will stand and what effect, if any, this new diagnosis will have on AP medication prescribing for children and adolescents.[6] The uncertainties surrounding the issue of diagnosis and treatment of bipolar disorder in children add to the importance of initiatives to improve the availability of timely information on these issues to support policy and program development at the State level, including the development of metrics and procedures for monitoring and assessing diagnosis and treatment patterns on a continuing basis. Although resource limitations in the current project precluded incorporating diagnostic information from medical claims in the exploratory measures, this represents an area of opportunity for follow-on efforts in the development and implementation of metrics.

Prescribing Patterns and Use of Mental Health Services

The volume of AP medications prescribed for children and adolescents has risen rapidly. During 1993-2002, medical office visits for children and adolescents that included AP medication prescribing increased approximately five-fold.[7] Although some studies have shown early indications that AP medication prescribing may be leveling off, use remains high compared to historical and cross-national patterns.[3] The simultaneous prescription of multiple agents, including those within the same class, often referred to as poly-pharmacy,[8] has also increased in both adults and children.

An important issue identified in discussions among the participants was the relationship of AP prescribing to the use of and access to appropriate mental health services. Although the strength of evidence varies across conditions and treatments, and published studies of medication efficacy vastly outnumber studies of the use of medication combined with non-pharmacological treatments for children and adolescents, many studies indicate that psychosocial interventions can be effective with conditions for which children are frequently treated with psychotropics.[9-16] In many instances, optimal treatment may involve the combination of psychosocial and psychopharmacological interventions, but more information is needed on the extent and characteristics of mental health services received by youth treated with medications such as

antipsychotics. Closely related issues concern the extent to which prescribing is preceded by a comprehensive mental health assessment, and the extent of appropriate follow-up monitoring which can be important to assess treatment response, reinforce adherence, and assess side effects such as weight gain. In response to these concerns, as discussed in Section 4 and the State Practices attachment, several of the collaborating States have developed, or are exploring initiatives, such as access to behavioral health consultations and second opinions to address these issues.

Safety

Studying the safety and efficacy of medications in children and adolescents is inherently difficult. There are informed consent and assent issues associated with conducting such studies. Rigorous studies of the effectiveness of APs in children and adolescents are of limited number, compared with studies of their effectiveness in adults. Because AP medications have unknown effects on the developing central nervous system, concerns have been expressed about their rates of use in children and adolescents.[17] Safety issues require analysis of the risk-benefit profile of these agents, specifically the trade-off of possible harm resulting from medications versus the harm of untreated disorders.[18] Safety in children cannot be inferred from adult data.[19] The definition of adverse events and degrees of symptom severity require standardization, as does calculating the NNTB (number needed to treat in order to benefit one additional child) and the NNTH (number needed to be treated to harm one additional child) so that researchers and clinicians may weigh relative costs and benefits of psychosocial and psychopharmacological interventions alone or in combination.[20] Pending clinical trials to establish safety and efficacy of drugs now being used off-label, clinicians must monitor children closely.[21]

Evidence-Based Practices

Most evidence of efficacy describes short-term symptomatic improvement. Long-term studies with rigorously defined functional outcomes for children and adolescents are needed. Effectiveness studies conducted in usual care populations and settings characterized by co-morbidity and service limitations are also needed.[22] For treatment of disruptive behavior disorders and pervasive developmental disorders, definitive data on long-term safety are lacking.[23] Many studies describe effects of mono-therapy, while in the community there is a high rate of combined pharmacological use.[24] More research is needed on the comparative effectiveness of psychosocial versus medication-based versus combined approaches across conditions,[25] although some studies have shown non-pharmacological interventions to be effective for particular disorders such as posttraumatic stress disorder,[26] depression,[27] and anxiety disorders.[28]

SECTION 2
Methods and Project Timeline

Background

The challenges of mental health services in Medicaid were discussed among State Medicaid Medical Directors, State mental health professionals and policymakers, and investigators from Rutgers' CERTs in June 2007 during an AHRQ-supported Medicaid Medical Directors Learning Network (MMDLN) meeting. Out of that discussion, MMDLN and CERTs participants developed a plan for a collaborative project to examine the use of AP medications for children and adolescents in Medicaid. Ultimately, a consortium of 16 States participated, representing a combined enrollment of 12 million children and adolescents in Medicaid.

Scope

As noted in the Introduction, the aims of the collaborative were to conduct exploratory analyses in each State on antipsychotic medication use rates and trends for children and adolescents in fee-for-service Medicaid using a comparable set of indicators that could "flag" possible safety and quality issues; provide a forum for discussion of policies and programs for optimizing AP medication prescribing among States; and develop a compendium of State practices classified by the contributing States as mature, promising and emerging according to a consensually developed classification matrix created for this project by the project participants that could be shared with other States to address AP utilization issues.

The project participants included State Medicaid Medical Directors and State mental health professionals and policymakers. Consensus development among participants was used to define the methodology and plan for data collection. The project included the following milestones:

- A series of informal discussions that generated the project plan.
- A discussion with Medicaid Medical Directors from as many as 23 States pertaining to the project scope and resource needs, which ended with 16 States agreeing to participate given the planned scope and timelines.
- The development of a standardized data dictionary with a subset of State participants.
- An informal data sharing agreement among 16 States to pull and share utilization and demographic data.
- Compilation of information on policies, statutes, and utilization controls related to mental health medications in a State.
- A set of definitions for State practices categorized as mature, promising, and emerging.
- A two-day meeting bringing participating States together to discuss data and trends.
- Calculation of pooled estimates from the State level analyses.
- Creation of a publication committee to write and review a resource guide for States wishing to understand their data and program characteristics.

SECTION 3
Data—Interpreting State Estimates of Utilization and Trends

Project Population

Medicaid covers 25 million children and adolescents less than 21 years of age through a number of programs including the State Children's Health Insurance Program (SCHIP), providing health care to some of the most vulnerable children in the United States. Health care services are provided through managed care contracts, or through FFS direct payment for services of health care providers. Although the mix of managed care and FFS differs by State, children with the most severe mental health issues are often enrolled in FFS, such as those who are in foster care, Supplemental Security Income participants eligible for Medicaid based on disability, and those with developmental disabilities,[29] a fact that is important to consider in interpreting data on this population.

We evaluated trends in the FFS Medicaid population (excluding the small number of Medicaid children and youth who are dually eligible for Medicare and Medicaid) in 16 States, comparing four years of pharmacy claims data capturing AP medications. The retrospective study concentrated on AP medication use but also captured claims for a broader group of prescription mental health drugs (MHDs) during calendar years 2004–2007. For the purpose of these analyses, MHDs included AP medications, attention-deficit hyperactivity disorder (ADHD) drugs, antidepressants, anxiolytic/hypnotics, mood stabilizers, and others, as defined by agreement among project participants. The Medical Directors agreed that these medications represent the typical utilization of mental health drugs in this population.

In 2007, the project involved a total Medicaid population of about 12 million children age 18 and younger. Thirteen States were able to report results for their foster care populations, totaling 285,756 children (Table 1).

AP Utilization

The tables below reflect pooled results from States' analyses of medication use rates (proportion with a filled prescription during the calendar year) for the years 2004 and 2007, for FFS children and adolescents aged 18 years of age or younger, in the 16 participating States. In 2007, a total of 193,178 of these beneficiaries received an AP prescription, representing 1.60 percent of the total FFS population under 19 years of age (Tables 1 and 2). Variation across States was considerable, ranging from 0.9 percent to 4.1 percent.

Thirteen States were able to report on their foster care populations. In this population in 2007, the rate of AP medication use was higher at 12.37 percent, in contrast to the 1.40 percent rate for children not in foster care (Table 2).

Male beneficiaries were more than twice as likely as female beneficiaries to be prescribed an AP medication (2.23 percent vs. 1.05 percent). AP medication use rates increased with age and varied between eligibility categories, ranging from 0.61 percent for SCHIP to 13.44 percent for the aged, blind, and disabled (ABD) population of children 18 years or younger.

From 2004 to 2007, the pooled AP medication use rate for children and adolescents in the 16 participating Medicaid programs increased from 1.45 percent to 1.60 percent in 2007, about a 10 percent relative increase. For foster care children and adolescents, the AP medication use rate increased (on a relative basis) by 5.6 percent between 2004 and 2007 (from 11.7 percent to 12.4 percent). In comparison, the rate among non-foster care children underwent a relative increase of 12 percent, from 1.25 percent in 2004 to 1.40 percent in 2007.

Table 1: Number of Beneficiaries in Study Population and Number Receiving Antipsychotic Prescriptions, 2007 and 2004

		2007		2004	
	States Reporting (n)	Total Clients (n)	Total AP Users (n)	Total Clients (n)	Total AP Users (n)
Total	16 States	12,063,667	193,178	12,037,000	175,069
Gender	15 States				
Male		5,215,718	116,528	5,314,288	106,236
Female		5,061,247	53,172	5,180,777	49,134
Age	16 States				
≤5		5,170,441	11,183	5,108,573	11,965
6-11		3,324,471	66,725	3,360,602	61,449
12-14		1,472,281	48,423	1,549,926	46,836
15-18		1,927,550	66,847	1,832,623	54,820
Eligibility[2]	14 States				
ABD[4]		410,325	55,149	379,462	45,164
TANF[5]		8,006,931	86,397	7,494,449	75,433
SCHIP[6]		1,117,344	6,849	681,384	7,144
Other		2,182,583	70,361	2,631,950	70,015
Foster Care[3]	13 States				
Yes		285,756	35,351	278,764	32,652
No		9,111,427	127,965	9,024,285	113,234

[1] For all States except Illinois. States reported 60,167 missing gender cases for 2007 and 62,340 for 2004.
[2] For all States except New Hampshire and New York.
[3] For all States except New Hampshire, New York, and Oklahoma.
[4] ABD=Aged, blind, and disabled children and adolescents aged 18 years or younger
[5] TANF=Temporary Assistance for Needy Families
[6] SCHIP=State Children's Health Insurance Fund

Table 2: Antipsychotic Medication Utilization Rates (2007 and 2004)*

	States Reporting (n)	2007 AP Use Rate (%) Pooled	2007 Min	2007 Max	2004 AP Use Rate (%) Pooled	2004 Min	2004 Max
Total	16 States	1.60%	0.90%	4.10%	1.45%	0.90%	3.33%
Gender[1]	15 States						
Male		2.23%	1.33%	5.61%	2.00%	1.26%	4.58%
Female		1.05%	0.58%	2.63%	0.95%	0.53%	2.17%
Age	16 States						
≤ 5		0.22%	0.02%	0.67 %	0.23%	0.05%	0.49%
6-11		2.01%	0.94 %	4.95%	1.83%	0.91%	4.00%
12-14		3.29%	2.05%	7.58%	3.02%	1.90%	6.56%
15-18		3.47%	2.00%	8.31%	2.99%	1.58%	7.24%
Eligibility[2]	14 States						
ABD[4]		13.44%	8.10%	23.39%	11.90%	7.35%	21.60%
TANF[5]		1.08%	0.30%	3.57%	1.01%	0.24%	3.45%
SCHIP[6]		0.61%	0.20%	3.28%	1.05%	0.23%	2.53%
Other		3.22%	1.05%	13.62%	2.66%	0.81%	33.54%
Foster Care[3]	13 States						
Yes		12.37%	5.80%	22.25%	11.71%	5.40%	23.67%
No		1.40%	0.69%	3.25%	1.25%	0.63%	2.72%

* Sum of AP medication users (numerator) in all States divided by the sum of clients (denominator) in all States.

[1] For all States except Illinois. States reported 60,167 missing gender cases for 2007 and 62,340 for 2004.

[2] For all States except New Hampshire and New York.

[3] For all States except New Hampshire, New York, and Oklahoma.

[4] ABD=Aged, Blind, and Disabled children and adolescents aged 18 years or younger.

[5] TANF=Temporary Assistance for Needy Families.

[6] SCHIP=State Children's Health Insurance Fund.

Medicaid Programs and Populations Served

Most States had a combination of FFS and managed care programs. The size of the FFS programs ranged from just over 12,017 beneficiaries to more than 2.45 million. Proportions of enrollees in different eligibility categories varied widely across States. For example, among FFS enrollees the proportion of children and adolescents in foster care varied from less than one percent to nearly half (data not shown).

Core Measures

In addition to the characterization of AP medication use for children and adolescents in the 16 Medicaid States, the project participants consensually identified five core measures of AP medication and total MHD utilization that served as preliminary measures to flag potential quality and safety issues in AP medication and total MHD therapy:

- Use of AP medications in children 5 years and younger;
- Use of high doses of AP medications;
- Use of multiple AP medications any time during a calendar year (including both concurrent and non-concurrent use);
- Maximal gap in days between AP medication claims, which may reflect medication adherence; and
- Use of multiple MHDs any time during a calendar year (including both concurrent and non-concurrent use).

Many of these core measures stem from the Texas Foster Care Study and from a consensus based on discussion among project participants on dose, age and poly-pharmacy standards, which participants agreed to accept as a base for the project. With respect to dose, the Texas study did not contain a dose recommendation for all ages for all the AP drugs. The participants agreed to use the dose recommendations for adolescents as a base for comparison across age, eligibility and other demographics (Table 3). Each measure was calculated for the calendar years 2004 through 2007 to allow for the evaluation of both pooled rates and trends (Table 4). In the pooled results below, we report on the results for 2004 and for 2007.

Table 3: Reference Levels Used for "High Dose" Measures

	Max Dose (mg per day)
Aripiprazole	30
Clozapine	600
Haloperidol	10
Olanzapine	20
Perphenazine	32
Quetiapine	600
Risperidone	6
Ziprasidone	180

Table 4: Study Population Exceeding Flags Indicating Potential Safety or Quality Issues

Flags		2007 Total Users (n)	2007 Average Use Rate (pooled)[1]	2007 Min (%)	2007 Max (%)	2004 Total Users (n)	2004 Average Use Rate (pooled)[1]	2004 Min (%)	2004 Max (%)
AP Medication Use in Children 5 years and Younger[2]									
	≤ age 5	11,183	0.22%	0.0%	0.7%	11,965	0.23%	0.1%	0.5%
≥ High Dose, Among AP Users[2,3]									
	< Max	214,866	91.1%	82.1%	98.7%	199,364	91.5%	83.6%	99.3%
	≥ Max	21,049	8.9%	1.3%	17.9%	18,602	8.5%	0.7%	16.4%
	≥ 2X Max	2,459	1.0%	0.0%	2.9%	2,754	1.3%	0.1%	2.6%
Multiple AP Medication by Age in a Calendar Year, Among AP Users[4]									
<19	One	142,498	79.5%	73.9%	83.6%	122,676	76.9%	72.5%	80.9%
	≥ Two	36,775	20.5%	16.4%	26.1%	36,914	23.1%	19.2%	27.5%
≤5	One	8,177	85.2%	80.3%	94.7%	7,374	83.3%	0.0%	88.6%
	≥ Two	1,433	14.8%	5.3%	19.8%	1,484	16.8%	0.0%	22.2%
6-11	One	50,398	80.4%	75.5%	85.1%	44,646	77.8%	73.3%	81.9%
	≥ Two	12,322	19.6%	15.0%	24.6%	12,739	22.2%	18.1%	26.7%
12-14	One	35,797	78.8%	72.5%	82.3%	33,039	75.9%	70.4%	81.4%
	≥ Two	9,643	21.2%	17.7%	27.5%	10,478	24.1%	18.6%	29.6%
15-18	One	48,125	78.2%	70.7%	85.1%	37,617	75.5%	71.4%	80.5%
	≥ Two	13,555	21.8%	14.9%	29.3%	12,233	24.5%	19.5%	28.6%
Maximal AP Gap in Prescription Claims (days), Among AP Users[5]									
	0	20,113	13.7%	2.4%	28.7%	19,950	15.1%	2.3%	34.9%
	>20	58,640	39.9%	23.3%	48.3%	51,810	39.3%	25.3%	49.1%
	>40	31,072	21.1%	9.4%	27.8%	26,860	20.3%	9.8%	26.9%
Multiple Mental Health Drugs Medications in a Calendar Year[6]									
	One	318,099	52.5%	37.2%	63.1%	316,714	51.9%	43.6%	61.5%
	≥ Four	66,224	10.9%	4.6%	19.9%	71,767	11.8%	4.7%	16.4%

1 Sum of users (numerator) in all States divided by the sum of clients (denominator) in all States.

2 Among children with ≥1 month eligibility to FFS Medicaid per calendar year.

3 Based on reference levels in Table 3 above. See *Use of Psychoactive Medication in Texas Foster Children, State Fiscal Year 2005.* Prepared by the Texas Health and Human Services Commission, Department of State Health Services, and Department of Family and Protective Services. June 2006.

4 Among children with ≥6 months eligibility to FFS Medicaid per calendar year.

5 Among children with ≥6 months consecutive eligibility to FFS Medicaid per calendar year.

6 Among children with ≥6 months eligibility to FFS Medicaid per calendar year.

Results

Use in AP Medications in Children Five Years and Younger. Overall, 11,183 children age 5 years or younger had a claim for an AP medication in 2007. This represents a use rate of 0.22 percent among children under 6 years old. Use rates ranged across States from 0.02 percent to 0.67 percent. The rates for 2004 and 2007 were similar (.23 percent in 2004 and .22 percent in 2007 for a slight relative decline of 4 percent).

Use of High Doses of AP Medications. These analyses are exploratory and did not utilize maximum dosage levels that varied by the child's age; future work is planned to refine these exploratory analyses. Since most of the AP medication uses for children and adolescents were off-label during the study period, and therefore FDA guidance on dosing ranges for these uses was not available, project participants agreed to use dosing thresholds developed by the Texas prescribing /provider community for a separate project (Table 3). There were 21,049 children and adolescents in 2007 with an AP medication claim at or above a maximum dose as defined by the Texas Foster Care report[30] (Table 2) (8.92 percent of children with ≥1 AP medication claim) and 2,459 children (1.04 percent of children with ≥1 AP medication claim) at or above two times the maximum dose (Table 3). There were large variations across States for high doses of AP medication claims, ranging from 1.3 percent to 17.9 percent at or above the maximum dose, and from 0.01 percent to 2.9 percent at or above two times the maximum dose. Compared with 2004, the rate of AP medication use at or above the maximum dose increased from 8.53 percent to 8.92 percent. Over the same time period, rates at doses at or above two times the maximum decreased from 1.26 percent to 1.04 percent. An appropriate source was not readily available for age-specific thresholds. Individual States examined their data on an age-stratified basis, interpreting results in the context of the age range, using more detailed dosing ranges ranging from less than one-quarter of maximum to more than five times maximum. Table 4 above provides a summary presentation of the pooled data, without age stratification. These pooled results constitute a conservative estimate of high-dose utilization, since a single threshold from the Texas foster care report (typically representing a maximum dose for 12 to 18 year olds) was applied to children of all ages.

Use of Multiple AP Medications During a Calendar Year. The use rate of multiple AP medications, defined as claims for two or more filled prescriptions for different AP medications any time during a calendar year, decreased from 23.1 percent of AP users in 2004 to 20.5 percent in 2007. Multiple AP rates reflect both concurrent and non-concurrent utilization. Concurrent use was not within the data-analytic capability of many States within resources available, so we used for exploratory purposes a simpler measure reflecting use of more than one AP medication within the calendar year (not necessarily concurrent). This measure often reflects the result of medication switches, such as those in response to side effects or lack of response, rather than intended poly-pharmacy. Collaborating States discussed the development of measures of concurrent use, building on measures that have been developed in some States. Further development of States' capacity to calculate more complex measures (e.g., concurrent use), and development and validation of such measures for use across States, was identified as an important area for follow-on work.

Maximal Gap in Days Between AP Medication Drug Claims. As a rough proxy for AP medication adherence, we calculated the maximum gap in supply between consecutive AP

medication claims within a calendar year. A gap of greater than 20 days was considered a potential marker for poor adherence. Pooled results for 2007 indicate that the proportion of AP medication users with a gap of more than 20 days was 39.9 percent with a range of 23.3 percent to 48.3 percent. Between 2004 and 2007, the proportion of children and adolescents with AP medication claims with a gap of more than 20 days remained largely unchanged (rate for 2004: 39.3 percent). Further development of proxy measures for adherence, and State capacity to calculate such measures, was identified as an important topic for subsequent work on quality metrics.

Use of Multiple Mental Health Drugs (MHD) During a Calendar Year. This project also examined utilization of multiple (four or more) MHDs any time during a calendar year. For the purpose of these analyses, MHDs included AP medications, ADHD drugs, antidepressants, anti-anxiety medications, mood stabilizers, and others, as defined by a consensus panel that agreed that these medications represent the typical utilization of mental health drugs in this population. As with use of multiple antipsychotics, we did not undertake to measure concurrent use as this was not within the data-analytic capacity of many States within the time and resources available. Between 2004 and 2007, the rate of MHD users with four or more MHDs decreased from 11.8 percent to 10.9 percent. Further work will explore concurrent use of medications from multiple classes.

Pharmacy Program Structures and Policies. States varied in terms of the populations covered, organizational structure, mental health contracts, statutes, and codes. To characterize differences between programs, States were asked to provide information about their structure. The questions were directed at categorizing State policies and practices related to AP medication management and included the following:

- Medicaid programs and populations served;
- Pharmacy program structure and policy development;
- Pharmacy policies; and
- Pharmacy program outcome monitoring and feedback.

This information was collected during the period from March 2009 through September 2009.

Policy Development and Controls. While pharmacy policy decisions were generally within the province of the Medicaid program itself, input from the State mental health agency or authority varied across States. Most States had one or more capitated contracts covering mental health service. However, in most cases costs of psychotropic medications were carved out from these capitations and paid by the State. A majority had a Maximum Allowable Cost (MAC) program for AP medications and received supplemental rebates for AP medications. States are federally mandated to have Drug Utilization Review (DUR) programs for Medicaid and some States also utilize Pharmacy and Therapeutics Committees to monitor the quality and efficiency of their Medicaid programs. There are a range of different controls and policies that States use to manage their pharmacy programs. Some policies are implemented by pharmacies at the point of filling the prescription through the use of prior authorization (PA), step therapy, or second opinion programs. Some States use prior authorization to enforce preferred drug lists (PDL). Other State policies are designed to improve the efficiency of the Medicaid program, including

generic substitution, generic first start, days supply restrictions (e.g., 15 days for first prescription, 30 days thereafter), pill splitting requirements, and frequency restrictions (e.g., once daily dosing). Some States had prospective policies in place to address quality and safety concerns, including age restrictions, dose restrictions, and combination restrictions. Many States had "grandfathering" or refill protections—allowing for existing prescriptions to continue to be filled when new policies were introduced. Table 5 provides a summary of these results.

Feedback to prescribers and mental health programs was a strategy employed by many States. A majority had used some form of prescriber report cards with individual prescriber AP medication utilization compared to a peer group. A few States incorporate AP medication metrics within their mental health contracts.

Table 5: Number of States with Pharmacy Controls/Regulations by Specific AP Medication

	Prior Authorization	PDL-Preferred	PDL-Non-Preferred	Provider Type Restriction	Step Therapy	Guidelines	Refill Protections	Second Opinions	Age Restrictions	Dose Restrictions	Combination Restrictions	Supplemental Rebates	Fixed State Maximum Allowable Cost	Generic First for AP(planning)	Total
First Generation AP Medications (FGAs)															
Chlorpromazine/HCL	0	3	0	0	0	1	2	0	1	3	2	1	4	1	18
Fluphenazine decanoate/HCL	0	3	0	0	0	1	2	0	1	3	2	1	6	1	20
Halperidol/decanoate	0	3	1	0	0	1	2	0	0	3	2	1	5	1	19
Loxapine HCL/succinate	0	3	1	0	0	1	2	0	0	3	2	1	5	1	19
Mesoridazine besylate	1	1	1	0	0	2	1	0	2	2	2	1	2	1	16
Molindone HCL	0	2	0	0	0	1	2	0	0	3	2	1	3	1	15
Perphenazine	0	3	1	0	0	1	2	0	1	3	2	1	4	1	19
Pimozide	0	2	1	0	0	1	2	0	0	3	2	1	2	0	14
Thioridazine/thioridazine HCL	0	3	0	0	0	1	2	0	1	3	2	1	4	1	18
Thiothixene/thiothixene HCL	0	3	1	0	0	1	2	0	0	3	2	1	5	1	19
Trifluoperazine HCL	0	3	0	0	0	1	2	0	1	3	2	1	4	1	18
Triflupromazine	1	2	0	0	0	1	2	0	0	2	2	1	1	1	13
FGAs Total	2	31	6	0	0	13	23	0	7	34	24	12	45	11	208
Second Generation AP Medications (SGAs)															
Aripiprazole	0	6	1	0	0	2	3	1	2	6	5	2	0	0	28
Clozapine	2	4	3	0	1	2	3	1	2	5	4	2	5	2	36
Olanzapine	3	3	4	0	1	2	3	1	2	6	5	1	0	0	31
Olanzapine + fluoxetine (Symbyax)	4	3	4	0	1	2	3	1	1	5	4	1	0	0	29
Paliperidone	4	4	3	0	1	2	3	1	1	6	5	1	0	0	31
Quetiapine fumarate	1	6	0	0	0	2	3	1	3	6	5	2	0	0	29
Risperidone	0	6	0	0	0	2	3	1	3	6	4	2	5	2	34
Risperidone inj.	1	4	2	1	0	3	3	1	3	6	5	1	0	0	30
Ziprasidone HCL	1	5	1	0	0	2	3	1	2	6	5	1	0	0	27
SGAs Total	19	77	24	1	4	34	54	9	27	91	70	27	60	17	514
Combined Total	21	108	30	1	4	47	77	9	34	125	94	39	105	28	722

*A number in a cell indicates the number of states that have a policy for the drug and/or class

Discussion and Limitations

Results of this multi-State effort to monitor utilization and potential safety issues for AP medication prescriptions using the claims systems of 16 States indicate that pharmacy claims can provide useful information across multiple States when using a common data dictionary, although further work is needed to increase and assure comparability across states. A key next step is to incorporate information from medical claims so that, for example, states can track diagnoses associated with antipsychotic prescribing. States' analyses provided them with information on several aspects of AP medication use in their state, including use in very young children, multiple AP medications prescribed for children in a calendar year, and a measure of refill gaps. Additionally, the data highlighted variations in both inter- and intra-State prescribing practices, although further analysis would be required to understand more clearly the contribution of case-mix and other factors in these variations.

Certain factors limit the general applicability of the data and conclusions that can be drawn from this project. The analyses for this project incorporated no clinical or diagnostic information. Some States had difficulty stratifying AP medication use by gender and eligibility groups (e.g., foster care). We were not able to examine other important potential factors related to the implementation or outcomes of AP medication use, including patient, family or provider preferences. The project was limited to children in the FFS Medicaid program and may not generalize to other populations. Outcomes related to other human services systems (e.g., juvenile justice activity, school attendance, etc.) were not measured and should be examined in future research. Our data appeared to show an increase in use of AP medications in some subpopulations, but additional information would be necessary in order to evaluate the medical necessity of these treatments. Further systematic analysis is planned in several States to examine the reasons for these observed trends.

Participating States described a wide variety of approaches to managing their pharmacy programs. Many States introduced new policies and programs over the study period including steps aimed at addressing issues of dose, age, and poly-pharmacy (i.e., multiple AP medications and MHDs) through prior authorization. Several of these initiatives were developed as a result of participation in this initiative, as discussed in Section 4. In general, the programs recorded by this study were too new to show a relationship to the 2004-2007 utilization data.

In interpreting these FFS utilization data, it is important to bear in mind the information discussed above (see Challenges section of the Introduction). As noted, data reflect populations of FFS beneficiaries whose composition varies across States, depending in part on varying eligibility procedures and managed care programs, and the measures were selected based on simplicity and feasibility of implementation by data analysts in the individual States under the resource and time constraints available for these exploratory analyses. We have not yet, for example, undertaken to measure simultaneous use of multiple medications or medication possession ratios as a proxy for adherence. The distributed data analysis model allowed multiple States to participate without the need to implement data use agreements, but it also limited the ability to perform iterative or multivariate analyses, adjust for clinical, eligibility, and other characteristics, or examine patterns in subgroups with different diagnoses, which are goals for subsequent stages of the work. While the data dictionary provided an overall template for State analyses, application of rigorous procedures for consistent distributed data analysis, such as use

of common statistical programs and coding, was not feasible. However, the pooled data provide useful insights into trends in antipsychotic use in Medicaid youth and variations across important subpopulations such as age groups, genders, and eligibility categories including foster care. The data also represent important first stages in a process intended to facilitate effective use by States of their claims data to understand and monitor treatment practices going forward, as well as to examine and compare treatment patterns and outcomes utilizing more refined and rigorous analytic procedures in subsequent collaborative work.

Notwithstanding these limitations, work on this project demonstrated the effective use of pharmacy claims data to explore utilization of AP medications and mental health drugs across multiple State Medicaid programs. Perhaps more importantly, it showed that State programs could work together to develop and use data definitions and measures for potential safety and quality issues (age, dose, multiple drug exposure, and adherence gaps) to highlight trends and monitor across State practices. This work has helped participating States begin to utilize their data more effectively to understand patterns of AP medication use in their programs. Identification of characteristics of and variations in prescribing for subpopulations of special concern, such as foster care children, has helped to focus efforts on quality improvement in these populations. The work has also highlighted the need for better-resourced collaborative efforts to develop and implement metrics and quality improvement initiatives. These efforts have the potential for considerable public health impact in improving pediatric mental health treatment and outcomes in the vulnerable populations served by the Medicaid programs.

SECTION 4
Interventions—Learning from State-Specific Practices

This section includes brief examples of State practices/programs that encourage appropriate prescribing of antipsychotic medication for children and adolescents. Detailed descriptions of the full 36 State practices can be found in the State Practices attachment. Every state contributed one or more practices. States described their practices using a standard template that included:

- Background
- Development timeline
- Program cost/ Funding source
- Measures results
- Outcomes
- Lessons learned

State practices were then categorized based on the type of broad implementation strategy utilized. The strategic categories with descriptive examples follow.

- **Policy:** Statute/administrative code modification related to AP medication prescription sharing.
- **Stakeholder Engagement:** Creation of multi-stakeholder task forces or workgroups to collaboratively address AP medication utilization.
- **Education/Marketing:** Coordination of efforts such as electronic handheld device programs, Web-based communications, consultation/training programs, consumer education, road shows, and academic detailing about AP medication prescribing.
- **Provider-Patient Feedback:** Patient/provider-specific feedback, report cards.
- **System Interventions:** Pharmacy requirements such as criterion-triggered second opinions, medication therapy management, rate setting, clinic-based quality improvement, prior authorization, electronic information exchange. Other interventions include PDL Programs, Maximum Allowable Cost/Rebate programs, Pay for Performance, and e-prescribing.

Finally, States ranked their practices as mature, promising, or emerging based on a State Implementation Strategies Classification Matrix (Table 2) that was developed for this project by the publications committee. The criteria are listed below:

- Evidence
- Maturity
- Dissemination
- Cost Effectiveness
- Access
- Acceptance
- Implementation

Table 1. State Practices			
State	**Strategy Description**	**Classification**	**Category**
Missouri	Treatment Adherence Program (TAP)	Promising	Policy
Washington	Mental Health Law and Confidentiality	Emerging	Policy
Washington	Generics First	Promising	Policy
California	Medication Therapy Management Services (MTMS)	Emerging	Stakeholder
California	CalMEND Collaborative Performance Improvement Project	Promising	Stakeholder
California	Stakeholder Engagement in Development and Implementation of CalMEND	Emerging	Stakeholder
Indiana	Mental Health Quality Advisory Committee	Promising	Stakeholder
Massachusetts	Working Group on Psychoactive Medication for Children	Emerging	Stakeholder
New York	PSYCKES, Clinic-Based Continuous Quality Improvement and Drug Utilization Review	Promising	Stakeholder
Oregon	Psychotropic Medication Utilization Management	Unclassified	Stakeholder
Texas	Psychotropic Medication Utilization Parameters	Promising	Stakeholder
Alabama	Stakeholder Engagement/Management & Consensus Building Interventions	Emerging	Education
California	Epocrates (Education/Marketing)	Promising	Education
Colorado	Medicaid Rx Review Program	Unclassified	Education
Massachusetts	Public Education	Emerging	Education
Missouri	Road Shows for Behavioral Pharmacy Management (BMP)	Emerging	Education
Missouri	Access to Consultation in Behavioral Pharmacy Management (BPM) Initiative	Mature	Education
Washington	Evidence-Based Mental Health Care	Mature & Promising	Education
California	Relationship of Poly-Pharmacy Rate to Practice Setting	Emerging	Feedback
California	Pharmacy Tool Kit	Emerging	Feedback
Colorado	Comprehensive NeuroScience (CNS) Program	Promising	Feedback
Maine	Academic Detailing	Emerging	Feedback
Maine	Report Cards	Emerging	Feedback
Massachusetts	Access to Consultation—MCPAP	Mature	Feedback
Missouri	Benchmark Reporting in BPM Intervention	Mature	Feedback
Oklahoma	SoonerPSYCH Behavioral Health Rx Management	Promising	Feedback
Oklahoma	SoonerCare Medical Risk Management	Emerging	Feedback
Washington	Provider Access Lines (Phone-Based Consultation)	Promising	Feedback
California	Use of the Web	Promising	Systems
Colorado	Use of the Web	Unclassified	Systems
Maine	Edits at Point of Sale	Promising	Systems
Missouri	Prior Authorization of ADHD Medications	Unclassified	Systems
New Hampshire	E-Prescribing	Emerging	Systems
New York	PSYCKES—Prior Authorization and Feedback	Promising	Systems
Pennsylvania	Prior Authorization of Olanzapine	Mature	Systems
Washington	Second Opinions	Mature	Systems

Policy

Statutes and Administrative Code on AP Prescription Sharing: *Washington*

- Washington State law required a release from the patient before sharing the mental health record. The mental health record definition extended to mental health medications, such that one prescriber of an AP medication could not know what another prescriber of a second AP medication was doing for a single patient unless a release was signed for both prescribers' records to be shared. In July 2007, legislation was passed which permits prescribers to share mental health prescription and diagnosis information contained in the medical claims file.

Stakeholder Engagement/Management

Task Force/ Working Group Creation: *California, Massachusetts, Texas*

Three States have either instituted or planned efforts to engage stakeholders in educational and/or therapeutic management activities:

- California established a client-oriented Clinically Informed Outcomes Management (CIOM) system within their broader California Mental Health Care Management (CalMEND) system with the goal of encouraging client participation in care plan management. CIOM is a Web-based, real-time electronic survey form executed at each visit before the client meets with the practitioner. Because the form is online, the results are immediately available to the practitioner during the visit.
- California established CalMEND, the California Mental Health Care Management Program in 2005. Since institution of the Web site, there has been an increase in both the number of visits and the average length of time spent on the site by stakeholders.
- Texas recognized high use of psychotropic medications among children in foster care and developed a focused program to monitor and optimize care in this population. They implemented personal health records for Medicaid clients who constitute the STAR health network and an online "passport" was developed that contains demographic data, immunizations, prescriptions, encounter data, diagnoses and medication allergies. Monitoring of these data permits review of cases outside of parameters identified by an interagency council.
- Massachusetts established a stakeholder-based work group to analyze pediatric utilization of psychotropic medications after the death of a four-year-old girl diagnosed with ADHD and bipolar disorder. The group identified practice outliers in psychopharmacological administration and in comprehensiveness of treatment. Trends and utilization are now being monitored as a statewide collaborative initiative.

Education/Marketing

Access to Consultation Programs: *Alabama, Missouri*

- To address the issue of the steadily increasing use of second-generation antipsychotics, Alabama convened a task force comprised of child psychiatrists, primary care physicians,

pharmacists, State agency representatives, and other payers to gather input from multiple sources and to design effective interventions. The task force agreed on two interventions: focused mailings to prescribers of any antipsychotic to children aged 0-17, and the educational telephone calls by child psychiatrists to prescribers of antipsychotics to children under the age of 5.

- Missouri uses its Behavioral Pharmacy Management system to analyze prescribing patterns for children and adolescents, after which letters are sent to prescribers offering consultation on best prescribing practices. Analysis of experience with this intervention showed that repeated messaging produced increased benefit over time as measured by an overall reduction in the percentage of outlier prescriptions by Community Mental Health Centers (CMHCs).

Use of the Web: *California, Massachusetts*

- California developed a Contract Drug List for Medi-CAL patients, and loaded its list to the mobile pharmacy database Epocrates in January 2007. The Epocrates software permits the viewing of coverage data as well as alternatives to drugs with utilization limits and constraints.
- Massachusetts separately maintains an online and hard-copy educational document for public education for parents, guardians and social workers. The document is periodically updated and focuses on both information about psychotropic medications and the broader context of the assessment of children's behavioral and emotional problems.

Feedback

Patient-Provider Feedback: *Colorado, Maine, Washington, Massachusetts*

- Massachusetts developed a program (Massachusetts Child Psychiatry Access Project [MCPAP]) to provide telephone consultative support by child psychiatry specialists to pediatricians. It is regional, flexible and supportive across all payers. The calls go to one of five regions determined by the home of the patient. This triage facilitates face-to-face consultation when indicated. The distribution also prevents specialists from becoming overburdened. The program has been in place since 2003 with strong acceptance by the pediatrician community.
- Washington began a telephone access consultation (Partnership Access Line [PAL]) similar to that of Massachusetts; however, the consultations are provided centrally by one source rather than regionally. The program has an ambitious evaluation component; the preliminary results indicate strong acceptance by the pediatrician community.
- Colorado engaged in a two-year program that used the services of a vendor, Comprehensive NeuroScience (CNS), to administer a Behavioral Pharmacy Educational (BPE) program. BPE provided educational alerts and letters to prescribers detailing information about the psychiatric medication utilization of their patients. Prescribing patterns post-intervention were followed and, if desirable changes did not occur, follow-up letters and face-to-face encounters with peer consultants were held.
- Maine initiated a report card program to inform prescribers by auto-fax of lapses in prescription filling. Also, the State's pharmacy management contractor (GHS) sends

quarterly reports to prescribers with at least 20 Medicaid patients, documenting the level of compliance with the PDL.

System Interventions

Criterion-Triggered Mandatory Second Consultations (Opinions): *Washington*

- Washington initiated a program to require a second opinion from a community psychiatrist when prescriptions for ADHD medications exceeded consensus-defined safety thresholds based on dose, combination therapies or age less than five. The program was well received in the prescribing community. Limits and guidelines are available at palforkids.com.

Hard Edits: *Maine, Pennsylvania, Tennessee*

- Maine established "hard" edits associated with their PDL for specific quality parameters including dosage, duplicate therapies, and potentially adverse drug interactions. These edits take place at the point of sale, disallowing the filling of a prescription without prior authorization. In addition, trial of at least one preferred antipsychotic is required beforé allowing use of a non-preferred SGA.
- Pennsylvania established a hard edit for prescription of olanzapine, requiring prior authorization for non-grandfathered prescriptions. The program began in 2005 and resulted in a marked decrease in the use of olanzapine; however, there was significant shift to the use of another branded SGA, aripiprazole.

Preferred Drug Lists (PDLs): *California, Massachusetts, Maine, New Hampshire, Pennsylvania, Washington*

- These States all have a version of a PDL. It is likely that other States also have a list of drugs that are either preferred or for which access is restricted in some way. The degree to which these lists are accompanied by sets of rules that balance access, quality and costs is presently undetermined. Specific rules to set the PDL lists differ by States although several States use the common evidence based reviews. For more information the reader is encouraged to contact these States for more specific details regarding policies and practices for setting a PDL.

Clinic-Based Quality Improvement: *New York*

- New York uses an inpatient computerized, Web-based quality and utilization review program, the Psychiatric Services and Clinical Knowledge Enhancement System (PSYCKES) for the Medicaid population, from inpatient setting to outpatient clinics. This tool is presently in use both in New York City and throughout the State, and is used to identify poly-pharmacy and use of PAs with high/moderate risk of metabolic side-effects.

Electronic Information Exchange: *New Hampshire*

- New Hampshire developed e-prescribing as part of its pharmacy benefit management services. The program is jointly administered by NH Medicaid and its pharmacy benefit administrator, First Health Services, Inc.

Characterizing State Implementation Strategies: A Classification Matrix

New mental health programs are implemented frequently but comparisons between programs are problematic due to differing maturity, scope, and trends in treatment patterns unique to each State. A matrix (Table 2) was developed by a subcommittee of this project comprised of members from Washington, Massachusetts, Minnesota, Alabama, and California. They invited States to classify their practices as mature, promising, or emerging (State Practices attachment). The purpose was to identify practices that have worked well or are likely to, and highlight them in a standard manner. The matrix does not "rank" or "rate" performance but simply creates a set of standards for States to help in evaluating whether another State's program can be implemented within resources and the current environment. The classification was designed to give a State the means to review each practice and consider its value based on the context of each State's needs.

A "mature" practice was defined as one with methods and data showing measured and validated results implemented across multiple sites—often statewide. "Promising" practices have been implemented at one or a few sites and have some data showing results. "Emerging" practices have been implemented in at least one site with only preliminary data available. Not every practice described has all the properties listed within a single column. For example, a "mature" practice may be disseminated to only a few implementers, possibly because of cost or difficulty in implementation. Another practice that has been taken up by many sites may have very little information available about its efficacy and thus remain a "promising" practice. In each case, assignment will depend on the thoughtful judgment of the person or person making the classification assignment.

There are undoubtedly other features of practices that have not been addressed by this matrix. There is always a tension between completeness and usability of the tool. The publication committee believes the features selected can help to identify useful health care improvement activities for consideration.

Table 2. Implementation Strategies Classification Matrix

	Mature Practice			Promising Practice			Emerging Practice	Unclassified
Evidence	Peer Reviewed. Published studies or detailed reports with methods and outcomes data showing clearly showing desired results. More than one study or report. Independent review(s).			At least one implementation site with data showing desirable results.			Implementation in at least one site. Data may be preliminary.	None
Maturity	Varies, but usually three or more years.			Varies. Usually within one-three years.			Less than one year to two years. Could be longer.	Usually less than year or could be in planning phase. Could be longer.
Dissemination	Multiple implementations (possibly of varying maturity). Geography depends on the practice.			One or more implementations, at least one site with data.			At least one implementation.	May still be conceptual.
Cost Effectiveness* Cost	Net Saving		Wash	Net Saving		Wash	Uncertain	Unknown
Quality	Increase or same		Increase	Increase or same		Increase or same	Increase or same	Unknown
Access	Substantial shifts in access in the desired direction.			Shifts in access in the desired direction.			May show shifts in access in the desired direction; or does not shift untoward.	Unknown
Acceptance* By Provider	Good	Fair	Good	Fair	Fair	Poor	Undetermined	Unknown
By Member	Good	Good	Fair	Good	Fair	Poor	Undetermined	Unknown
Implementation	Straightforward. Minimal review. Minimal additional costs. Most resources already in place.			May be straightforward, or may require agency or legislative review. May require budgetary increases and/or additional resources.			Significant perceived barriers of cost, acceptance, review and/or resources.	Unknown, but barriers expected.

*Requires both elements.

SECTION 5
Change Management—Using the Resource Guide to Develop AP and MHD Quality Strategy

Introduction

Measurement is a critical component of quality improvement. There are numerous efforts to develop consensus on standardized measures for quality improvement in mental health care. The National Association of State Mental Health Program Directors Research Institute has implemented standardized measures across nearly all State psychiatric hospitals in the United States.[31, 32] The Joint Commission recently developed a set of measures to assess the quality of inpatient psychiatric care in both the public and private sector.[33] The National Quality Forum is working to develop consensus on the best and most important measures across sectors and settings, reflecting a diversity of conditions, treatments, populations, and quality concerns.[34] Thus far, they have identified over a dozen measures for mental health.

There is however, a need for additional outpatient-based measures for children and adolescents. The *Report and Resource Guide* seeks to provide information that will contribute to a State's efforts to implement quality improvement initiatives aimed at these objectives. Various sections in this guide address distinct information needs and State users. Senior leaders are responsible for making the case for mental health quality improvement and taking action (Sections 1, 4, and 6) while program staff would need to provide the information necessary to develop and implement a quality improvement strategy (Sections 2, 3, and 5).

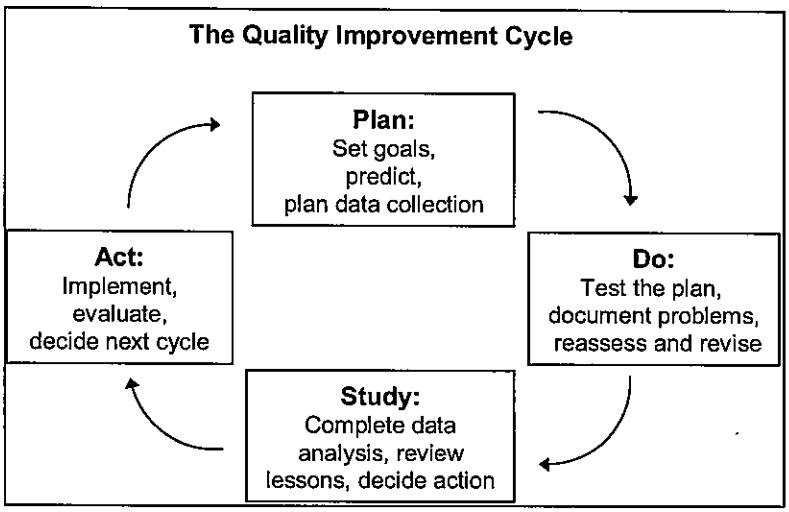
This Section discusses a model for quality improvement, presents a case study, discusses evaluation and offers a model for evaluation purposes. It also discusses how State leaders can begin to develop their own State-specific strategies to collect, analyze, and compare the data on AP use in children within their State.

Plan-Do-Study-Act (PDSA) Model

The PDSA is a time-tested quality improvement tool for guiding quality enhancement projects of all types (Figure 1). The PDSA model conceptualizes the continuing cycle of improvement. Its steps for effective quality improvement include:

- **Plan:** Set the goals of the quality improvement cycle—questions, predictions, data to be collected, and the who, what, when, and where of the project.
- **Do:** Carry out the plan and document problems and unexpected observations.
- **Study:** Complete the analysis of the data, compare to predictions, and summarize lessons.
- **Act**: Determine changes to be made and decide what will happen in the next cycle.[35]

Figure 1.



Source: Adapted from Langley G, Nolan K, Nolan T, et al. *The Improvement Guide: A Practical Approach to Enhancing Organizational Performance.* San Francisco: Jossey-Bass Publishers, 1996.

The PDSA cycle usually applies at the point of production, in this case to the front-line of health care at the point of care. The concept also can be applied to the quality improvement role of State leaders. Drawing on insights from State quality improvement activities around the use of AP medications in children, State leaders might consider a "Partner-Plan-Do-Study-Act" model.

- **Partner:** Decide who are the strategic partners of quality improvement and recruit them to the project—champions in health care production, stakeholders (e.g., consumer/patient groups, health care professionals, purchasers, health plans, and topic experts), and key State leaders and agencies (e.g., visible champions, child mental health experts, program planning/evaluation staff, and quality improvement experts). Is the group large enough to include key leaders and perspectives, yet small enough to be productive?
    - For example, some States have local collaboratives for mental health quality improvement that address local issues while other States have a Statewide quality collaborative that include a variety of stakeholders along with key staff of relevant State agencies.

- **Plan:** The goals of a project will be broad in the context of statewide activities because many partners and processes will need to be involved. What does the group predict are the current obstacles to quality care? How will the goals be put into action? What data need to be collected to prove that the changes are indeed improvements?
    - For example, some States use the process to address a specific issue like AP use in clients under 5 years of age while others use it to assist in setting statewide polices, obtaining buy-in for guidelines, prior authorization criteria and policies for generic use.

- **Do:** Test the plan and document problems and unexpected observations as data are collected. Initial plans seldom produce desired results the first time. Pilot test the ideas of the group with front-line health care programs, providers, and consumers. Reconvene the partners and discuss successes and problems.
    - For example, see Section 6 and Epilogue for descriptions of how States have used the project data and are implementing utilization control.

- **Study:** Complete the data analysis, compare the results to predictions, and summarize lessons learned. Do the test results convince the partners that full-scale implementation will be successful? Because the scope of activities may be broad and costs may be involved, the planned action should be based on reasonable data and results.
    - For example, the State practices attachment and Section 4 are concise descriptions of the 36 practices being addressed in 16 States.

- **Act:** Determine the changes to be made. Implement the changes statewide or in a district. Continually assess those changes through data collection and analysis. Are the changes working? What will happen in the next cycle?
    - For example, the case study below is useful in understanding how one State acted on an issue and used the PDSA model to solve an issue with mental health drug prescribing.
    - The PDSA model can be applied to the context of State leadership in quality improvement. The actual approaches and actions that States take will be as varied as the examples that appear in Section 4 of this guide.
    - Additional tools include:
        - The Health Care and Workforce Improvement tools (http://www.qaproject.org/resourcesintro.html).
        - The Institute for Healthcare Improvement (IHI) breakthrough series focuses on change at the provider level, but is an important approach that State leaders should understand for developing change agents (http://www.ihi.org/ihi).

Case Study

Partner

Washington's State Department of Social and Health Services worked with the psychiatric community to improve prescribing practices of medications for ADHD in children and adolescents receiving FFS Medicaid services. Their process follows the PDSA model.

Plan

Beginning in 2004, Medicaid workers in Washington worked with community mental health and primary care providers to create consensus based safety thresholds for prescribing ADHD medications. These thresholds included age (less than 5 years old), combination use (use of two or more ADHD drugs for more than 30 days), and high doses of amphetamines or dexmethylphenidate (greater than 60 mg), methylphenidates or atomoxetine (greater than 120 mg), methylphenidate patch (greater than 30 mg), or Lisdexamfetamine [L-lysine-D-amphetamine]

(greater than 70 mg). The group approved thresholds and guidelines, which served as the basis for requiring second opinions whenever a child or adolescent was prescribed a drug which exceeded one of the thresholds.

Do

Beginning in May 2006, Washington Medicaid contracted with three children's medical centers and their pediatric and adolescent psychiatrists or developmental pediatricians to conduct second opinions via record reviews. A second opinion was required for combination use of ADHD medications for more than 30 days (except in instances of titration, tapering and crossover between medications). Refills of medications in excess of thresholds were allowed during record review; however, first-time prescriptions that exceeded thresholds were not filled while under review. If additional questions arose during the record review, the second-opinion provider often held a consultation with the prescriber via telephone.

Study

Washington Medicaid payment system contains patient-level information on use, demographics, and cost. Researchers were able to analyze this information both before (May 2004–April 2006) and after (May 2006–April 2008) the second-opinion process was put into place. Information on this process was collected from ADHD worksheets containing the prescribing rationale and second-opinion outcome (i.e., approval, denial, or alternative). The resulting analyses reflected that 5.35 percent of ADHD prescriptions exceeded thresholds, requiring 1,046 second-opinion reviews. Just over half (51.4 percent) of these resulted in a prescription adjustment. High doses of ADHD medications were reduced by 53 percent, in combinations by 44 percent and for patients less age 5 years and younger by 23 percent. The savings to Washington Medicaid as a result of the program was $1.2 million.

Act

One key result of the ADHD second-opinion program was the extension by the Washington State legislature of this process to SGA medications prescribed to children and adolescents. Medicaid and a medical center are now required to measure prescription utilization as well as long-term outcomes such as symptom reduction, permanence of placement for children and adolescents in foster care, school performance, graduation rates, juvenile justice activity, and overall health benefits.[36]

Developing a State Strategy

Implementation Teams

A few States are currently utilizing implementation teams to promote the use of evidence-based practices. Key team members could include individuals who know and/or have used the interventions or practices that need to be implemented, are skilled in implementation methods, and engage in continuous quality improvement. Team members also need to know how to apply usability testing and the PDSA cycle described above. In addition, the implementation team

would also include intermediaries—opinion leaders and change agents. Opinion leaders implement the new practice, which helps to overcome caution about risks and costs, and can help persuade others to take up the innovation. Change agents create demand for new practices, reduce barriers to adoption, and act as bridges between technical experts and potential users.

Getting Started

The six steps in the evaluation process may vary as to when they are carried out, though one step usually lays a foundation for the next. Steps will be repeated as results become clear and new issues arise. Each step serves to ensure the effectiveness of the evaluation.

- **Engaging stakeholders** is essential to ensure that the evaluation addresses the important elements of the program and that the evaluation is used. Several States have regular meetings with mental health leaders or use the Drug Utilization Review (DUR) committees as a sounding board to action.
- **Describing the program and goals** helps to detail strategies and provide opportunities for consensus building. Some States have charters and business plans that address AP use; others engage the community and legislature in setting safety standards and guidelines.
- **Focusing the evaluation design** addresses the greatest issues of concern. This step includes identifying the purpose of the evaluation; defining the users and usefulness of the evaluation; listing stakeholders' questions that need to be addressed; establishing methods to ascertain information upon which the evaluation will be based; and developing consensus around particular roles and responsibilities pertaining to the evaluation. Some States have started slowly to build trust and credibility. There are examples in Section 4 where evaluation and design have led to community agreements on prior authorization criteria and generics first programs for APs.
- **Gathering credible evidence** contributes to the robustness of the evaluation. Developing credible evidence involves defining appropriate indicators, identifying legitimate sources of information, ensuring the quality of data gathered, and aligning the infrastructure for collecting evidence with the environment (and individuals) from which the information is gathered. This is where the data dictionary allows a State to recreate the data described in Section 3. Using common data definitions, flags can be created, areas of concern can be noted, and then brought back to the committee. Some States have used this data in DUR presentations, targeting outlier counties for interventions and profiling prescribers.
- **Justifying conclusions** is important to ensure that the evaluation will be used. When consensus is reached regarding the goals and strategies of the program, when the values of the evaluation are aligned, and when the evidence gathered is credible, then conclusions will naturally be justified. At this point, conclusions and recommendations can be made using data. In addition, data can be used as an ongoing quality improvement program and contracting expectations. Some States have used the data and committees to assist in setting codes and informing legislators on statutory changes to improve quality and safety related to AP use.

- **Ensuring use and sharing lessons learned** includes designing mechanisms for feedback and dissemination of the information gained in the evaluation. For example, the data dictionary contains a process to measure and display county-to-county variations based on the flags.

Other Ideas for State Action

For some State leaders, broad statewide quality improvement efforts may seem unattainable or unrealistic, given the scope of their responsibilities or the status of their budgets. There are, however, other activities that help raise awareness of quality improvement and build support over time for larger quality improvement efforts. Some options include the following:

- Talk with other organizations and individuals about ways to improve care in your State (e.g., staff in the State health department, advocacy organizations, health care professional organizations for mental health, as well as providers and health plans).
- Convene a conference or advisory group of experts in the State to discuss strategies for quality improvement or work with one that already exists.
- Hold/participate in a legislative hearing or town hall meeting on health care quality in the State.
- Participate in State efforts to raise public awareness about the use of antipsychotic medications in children.
- Consider public-private partnerships and public-private collaboratives to address quality improvement.
- Examine ways for State employee health programs and Medicaid offices to work together to improve care.
- Help establish a program for Medicaid clients by partnering with private sector organizations for services.

SECTION 6
Lessons Learned—Moving Forward

Summary of Project Findings

The Antipsychotic Medication Use in Medicaid Children and Adolescents project was the first to assess and compare AP medication use in Medicaid children and adolescents across a large group of collaborating States. The project demonstrated that State Medicaid programs could agree on a set of core measures to flag potential issues in the safety of AP medication and MHD therapy, and could develop a framework for each State's analysis of its data on medication use. States shared a wide variety and number of approaches being developed to improve the quality of prescribing. Almost all the approaches showed some degree of effectiveness to change prescribing practices, improve quality or mental health outcomes. There was no single essential approach—each State crafted interventions based on its specific environment. Practices in this area are evolving and will continue to change and grow. The sharing of State data and practices allow for analysis of trends, turning data into information, prioritizing issues, learning from others and benchmarking to achieve a more reasonable assurance of success.

Implications for the Future

Standardizing Measures Across States

The paucity of nationally standardized data definitions and quality measure definitions applicable to the Medicaid population is an obstacle for Medicaid health care improvement. Pharmacy claims data were chosen for this initial set of exploratory analyses in part because there is greater standardization of data elements in pharmacy benefit programs and minimal claim lag. While a data dictionary provided definitions for a common set of indicators, variations in details of inclusion criteria, mix of eligibility categories, differences in diagnostic profiles and clinical characteristics, and other cross-State variations still existed. State data analyses were conducted separately by statistical programmers at the various sites, using separately developed programming code that varied across States. The project required the investment of a substantial amount of staff time at the State level for reruns of initial tables due to such issues as variations in claims systems, data element definitions, and the need to resolve apparent inconsistencies. Future projects would benefit from broader standardization and testing of data elements, measure definitions, and data collection instructions.

Achieving meaningful nationwide improvements in Medicaid will require both Federal and State commitment as well as an investment of time and effort to develop and use standardized measures and benchmarks.

Evaluating Clinical and Functional Outcomes in Claims Data and Beyond

This project focused on a relatively narrow core of descriptive measures related to utilization patterns and did not address the more complex issues of clinical outcomes such as medication side effects or patient functional status. These exploratory analyses do not provide a basis for determining optimal utilization rates that are consistent with optimizing patient outcomes. It was also not possible to determine the effect that interventions to reduce pharmacy utilization had on

utilization and costs in other health care service areas. Multiple methods will be required in future work to better improve understanding of changes in total health care service utilization and costs, as well as clinical outcomes. Ideally, future efforts would include cycles of measurement, intervention, and remeasurement.

Adopting Structured Approaches to Quality Improvement

Because this project was a snapshot of independent, State-specific practices, it proved difficult to understand the impact attributable to particular interventions. Most of the participating States used multiple interventions that overlapped. Adopting a more structured approach to quality improvement across States could accelerate the identification of interventions that have an impact on AP medication prescribing practices and health outcomes. Within States, adopting a standardized model for quality improvement with measurement of clinical outcomes, in addition to AP medication prescribing practices, would promote the identification of those interventions most effective in improving patient outcomes.

Sharing Lessons Learned

Bringing the Medicaid Medical Directors together on a focused project markedly increased their awareness of the varied number and breadth of innovative interventions targeted at the prescribing practices of AP medications for children and adolescents. Project participants benefited greatly from the work effort by developing an in-depth understanding of new practice options and differing potential measures of outcomes. The project highlighted the need to establish ongoing mechanisms for sharing new learning in this rapidly growing field.

Benchmarking

Although project participants remarked on the potential benefits of benchmarking, most agreed that further work is needed to translate these measures into metrics suitable for provider feedback and dissemination of State comparative information. Engaging stakeholders in the design and implementation of future improvement initiatives should increase acceptance of the validity and meaningfulness of results. In addition, State leaders may want to work incrementally toward transparent and comparative benchmarking by developing community-wide agreement on how such data are to be used.

Pay for Performance

Contractual arrangements play a variety of roles in the provision of clinical services and pharmacy benefits in Medicaid programs. When contracting for pharmacy benefits and overseeing managed care providers, State Medicaid programs could explicitly require effective practice improvement interventions and attach fiscal benefits and penalties to their performance. Using the data and flags outlined in this project, a State can dialogue with providers and contractors concerning measures and goals that could fit into a contract or pay-for-performance program.

Investing in Databases

Health care system administrators, including State Medicaid leaders, are responsible for seeing that the populations they serve receive adequate services within the usual standard of care while improving both quality and costs, which add to the value of mental health care. Health care system administration is, at its best, a population-based form of evidence-based medicine. Evidence-based medicine is defined as "the integration of the best research evidence with clinical expertise and patient values."[37] State leaders can optimize their decisionmaking by investing in and developing quality and outcome information from their claims systems to complement and enhance clinical research evidence and expert consensus.

Project participants found great value in learning about State's actual service utilization and practices, and felt it greatly complemented the repertoire of evidence-based interventions developed in more idealized research settings (see State Practices attachment on actions in response to participation in this collaborative initiative). As noted in the Epilogue, to capture the impact and consequences of State participation in this project, all States were contacted by phone between September and October of 2009. Brief interviews were conducted with State point persons and notes were taken during these meetings. Quotes were summarized and reviewed by States to check for accuracy and States were provided an opportunity to update this information in March and April of 2010. For many States participation in the MMDLN project furthered initiatives related to psychotropic prescribing practices for children that were already underway. For other States, participation was the first step toward addressing this quality concern. Examples of the utility of participation (Epilogue) included helping to identify quality indicators to incorporate into existing programs such as prior approval programs, quality improvement collaboratives, drug utilization review procedures, and consultation programs; identifying treatment disparities for populations of special concern such as foster care children; identifying quality issues of special concern for the State; communicating concerns with stakeholders; lending credibility to quality improvement initiatives already underway; and supporting the development of new policy and legislation.

Conclusion

This project provided an opportunity for States to come together to discuss their experience with policies and practices related to the challenging issue of prescribing AP medication to children and adolescents, and a framework for identifying issues in their AP utilization trends. It also helped participating States to make more effective use of their own data to monitor and address issues of AP medication prescribing by providing a collaboratively agreed upon set of core measures and a standardized approach to data collection and analysis. Most important, this project demonstrated the value of working collaboratively to more broadly measure and monitor treatment practices for children and adolescents who suffer from a psychiatric disorder. Ultimately, the objective of this project is to foster more collaboration and information sharing among States to identify and develop best practices that provide America's children and adolescents with the right care at the right time for the right reasons.

EPILOGUE
State Actions Taken as a Result of Participation in the Antipsychotic Medication Use in Medicaid Children and Adolescents

Outcomes of Participation

To capture the impact and outcomes of State participation in this project, all States were contacted by phone between September and October of 2009. Brief interviews were conducted with State point persons, and notes were taken during these meetings. Quotes were summarized and reviewed by States to check for accuracy (Table 1). Examples of the utility of participation included:

- Lending credibility to efforts already underway;
- Bringing special attention to health disparities, such as those involving children in foster care, or regional variation;
- Identifying quality indicators to incorporate into existing programs such as State DURs, PA programs, quality improvement collaboratives, clinical decision-making supports, and consultation programs;
- Defining quality indicators, for example in high dose parameters where therapeutic doses have generally not been defined;
- Offering examples of State programs for improving quality of care;
- Use of multi-State comparison data, based on a standard set of definitions, that help to identify quality concerns for a State and may assist in implementing new initiatives;
- Use of multi-State comparison data to increase awareness of quality concerns and practice trends (e.g., rising use of AP for children) among stakeholders, policymakers, and community providers; and
- Supporting development of new policy and legislation.

Table 1. Outcomes of Participation Table	
AL	▪ This project was aligned with efforts already underway in Alabama to address antipsychotic use in children. Participation in the project lent further credibility and support to these efforts and provided an opportunity to collaborate with other States.
	▪ A task force has been established to review AP use (although underway when the project began, the project reinforced the need).
	▪ Two primary interventions have been developed: (1) focused mailing to prescribers who have clients less than 18 years of age on an antipsychotic; (2) peer-to-peer phone calls conducted by a child psychiatrist with any physician with a client less than 5 years old on any AP to discuss the use of these drugs in children.
CA	▪ The project provided an approach to examine dosing of antipsychotics in children, where therapeutic doses had generally not been defined. These quality indicators may be adopted by the Department of Health Care Services (DHCS) to reduce variation.
	▪ The project enhanced the activities of CalMEND (California Mental Health Care Management), a collaborative quality improvement initiative between DHCS and Mental Health to improve antipsychotic prescribing practices for adults and children.
	▪ Beginning in 2007, CalMEND carried out a Performance Improvement Project (PIP). This multi-county collaboration led to the development of a set of quality measures for antipsychotic use in adults and a "pharmacy toolkit." As part of PIP, optimum ranges for dose, medication adherence (gaps between prescriptions), access to medication, and poly-pharmacy indicators were developed for use in treatment of adults with seriously mentally ill (SMI). ▪ Based on this work, the antipsychotic utilization review/management quarterly report of the California Department of Health Care Services Pharmacy Benefits Division includes the measures for adults with SMI. In addition to adult measures, the demographic analyses include children and adolescents (age, ethnicity, geographic location by counties). ▪ In their next quarterly report, California's Pharmacy Benefits Division plans to highlight the children and adolescent population using the AP measures. It is hoped that use of these measures will begin the process of vetting and adopting the AP measures by DHCS.
CO	▪ The initiation of this project coincided with Colorado's desire to examining antipsychotic use in children. Participation in this project provided a set of indicators to examine and examples of State programs for improving quality of care.
	▪ Since the project began, Colorado has introduced a PDL for stimulants, antidepressants and atypical antipsychotics.

IN	▪ As the first multi-State comparison of AP use in children, the project provided the basis for comparison to other States, their policies, and practices.
	▪ Project data will be shared with the Mental Health Quality Advisory Committee (MHQAC) as they begin discussion of mental health drug use in children.
	▪ The MHQAC was created during the 2005 session of the Indiana General Assembly to develop guidelines and programs to allow open and appropriate access to mental health medications, provide educational materials to prescribers, and to promote appropriate use of mental health medications. This project will align with the MHQAC objectives for 2010.
MA	▪ Massachusetts has two Medicaid/Department of Mental Health workgroups devoted to psychopharmacology; both workgroups have been influenced by work of MMDLN and this project. ▪ The first workgroup, concerned with all ages, has developed an emerging program of PA for certain psychotropic drugs, supported by educational letters to prescribers, and informed by the efforts of the MMDLN project. ▪ The second workgroup focuses on Medicaid members under the age of 19, and has followed the work of the MMDLN closely. This committee works with both managed care organizations (MCOs) and non-MCO members for data collection to support decisionmaking. While MCO and non-MCO data may vary, the committee has sought to have its data collections as close to the MMDLN as possible. This effort is in direct response to the MMDLN effort.
ME	▪ Maine relies heavily on academic research and national surveys as sources of validation in its work to develop consensus for policy implementation (example, Dartmouth Atlas, health disparities research) and found participation in the project helpful for a peer-level comparison. ▪ The project provided the opportunity to view Maine's performance and policies in comparison with other States, making participation "tremendously useful."
	▪ The project informed quality improvement and reinforced the need for data collection, review, and reporting in an ongoing fashion for the child and adolescent population.
	▪ Maine has used the project and its key questions as a template to review State policies.

MO	▪ The study was helpful to focus Missouri's efforts in understanding AP use in kids.
	▪ Prior to the project initiation, Missouri had been focusing on high dose and poly-pharmacy but had overlooked the rapidly increasing use of AP in the youth population. Missouri has refocused its interventions to include general AP use in kids.
	▪ As a result of data, policy, and practice review related to AP in kids, Missouri has identified an opportunity to start a dialogue with P&T and DUR. The resulting information will be presented to the General Assembly to begin a legislative dialogue around the topic.
	▪ As a result of this study, Missouri conducted a study on foster children (wards of State) and medication use in the cohort.
	▪ The project was helpful in understanding the practices among participating States to confirm current best practices and activities.
	▪ Missouri viewed the project as a collection of best practices related to psychotropic medication use in children.
NH	▪ New Hampshire has used the project as a launching point for work on AP use in children.
	▪ Based on the project, New Hampshire has taken action and brought new initiatives to work groups focused on AP use in kids.
	▪ Based on work with the project, New Hampshire has identified indicators to flag for children on AP, reviewed measurement indicators, identified additional measurement strategies, reviewed peer controls, and is considering the use of second opinions and step therapy.
NY	▪ Project participation has increased awareness of prescribing for children in foster care and prompted a series of meetings among the Department of Health (DOH), the Office of Mental Health (OMH), and the Office of Children and Family Services (OCFS), and some exploratory data analysis.
	▪ The Psychiatric Services and Clinical Knowledge Enhancement System (PSYCKES), a Web-based platform to support quality improvement efforts in Medicaid, will incorporate the project indicators. The auspices of the AHRQ–MMDLN project helped to promote acceptance of the quality indicators, for example in selecting and defining dose parameters.
OR	▪ The project provided both new and renewed interest in AP use in kids including legislative action, PDL development, and DUR changes.
	▪ As a result of participation in this project, and in alignment with efforts already underway in Oregon, a review of psychotropic medication use in foster children resulted in passage of new 2009 State legislation. This statute mandates annual review of medications for foster children taking more than two psychotropic medications and

	requires a mental health assessment prior to issuance of any antipsychotic medication.
OK	▪ As a result of participation in this project, Oklahoma has developed a director-level workgroup between the Department of Mental Health and the Medicaid agency.
	▪ Oklahoma was concerned with its prescribing practices and health status ranking, as previously they had exhibited poor performance on select health indices as compared to other States. The project provided an opportunity to evolve policies and gain awareness into the work of other States.
	▪ Oklahoma would like to continue its involvement in multi-State work groups for peer comparison and best practice review.
PA	▪ Pennsylvania found participation in the project very useful.
	▪ The data requests allowed for directional data analysis. Pennsylvania then followed with "deep dives" into the data for further review of AP use and populations served. As a direct result of the data pull for this project, Pennsylvania looked further into foster care and use of AP. ▪ From data review, Pennsylvania confirmed concerns surrounding (1) short-term use of AP in foster care, (2) low dose of AP for non-diagnosis specific treatment (no mental health diagnosis to support use), (3) observation of non-guideline based use for AP for difficult behavior disorders and substance abuse treatment (withdrawal), and (4) episodic use for conduct disorders and sedation for ADHD at night (quetiapine). ▪ Pennsylvania conducted a cohort review for a two-year period to confirm hypothesis ▪ Based on this review, Pennsylvania found a significant number of children were prescribed antipsychotics for episodic non-guideline based use (generally used as sedation agents).
	▪ The project reinforced Pennsylvania's implementation of required PA of all requests to use APs in children under 6 years of age.
TN	▪ At time of project initiation, Tennessee had a parallel interest in reviewing use of psychotropic medication in children. Prior to project initiation, Tennessee had instituted controls on psychotropic use in children.
	▪ Historically, Tennessee has a high drug utilization rate. Based on this, Tennessee was interested in learning more about other State's prescribing rates and populations.
	▪ While there were no "ah ha" moments, the project outcomes helped to validate the work through multi-State comparisons. The project served as a litmus test to determine if limits have worked as intended.

WA	▪ At time of project initiation, Washington had set up two mental health work groups to address the use of psychotropic and mental health medication in children and adults. Prior to project initiation, Washington had instituted controls on ADHD, mood stabilizers, and antidepressant use in children with some published success in the use of second opinions for ADHD drugs (too young, too many, too much).
	▪ Historically, Washington has a low drug utilization rate; however, based on comparisons with other States, medication gap rates are high. Washington is interested in learning more about other State's prescribing rates and how to improve adherence. WA plans to reach out to States that performed well on this measure to explore incorporating their programs.
	▪ While Washington's total rates were good in comparison (except for gap in prescriptions), the project outcomes helped to validate the work and prioritize activities. In addition, the project has help to galvanize the State into several new statutes (HB1088, HB5892, HB5773) as well as several new programs such as a "generics first" program for new AP starts.

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STATE PRACTICES

36 State Practices to Improve Antipsychotic Medication Safety and Quality

Measuring Antipsychotic Medication Use in Medicaid Children and Adolescents: 2004–2007

Medicaid Medical Directors Learning Network (MMDLN)/Rutgers CERTs

June 2010

Introduction

This attachment previews 36 specific practices/programs that encourage appropriate prescribing of antipsychotic (AP) medication for children and adolescents. Practices are categorized as policy, stakeholder engagement, education/marketing, patient-provider feedback, and system interventions. Each practice was rated by the contributing State based on a State Implementation Strategies Classification Matrix that was developed specifically for this project (see the Matrix below in Table 1 and the description in Section 4 of the *Resource Guide*). Each State wrote these short summaries based on this matrix and the summaries have not been edited for content.

These detailed descriptions use a standard template that includes: background, development timeline, program cost/funding source, how measured, outcomes, and lessons learned. In addition, practices were classified by the contributing State as mature, promising, emerging, or unclassified. A "mature" practice was defined as one with methods and data showing measured and validated results implemented across multiple sites—often statewide. "Promising" practices have been implemented at one or a few sites and have some data showing results. "Emerging" practices have been implemented in at least one site with only preliminary data available. "Unclassified" programs lack several elements or were too new at the time of this writing to classify.

While local statutes, codes, communities and other variables that influence programs, readers are encouraged to review each practice and determine whether or not it may be a fit based on their AP and mental health issues as well as unique State characteristics. Contact information is provided for each State practice.

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Missouri: Treatment Adherence Program (TAP) Promising Practice

Background

The main objective of Treatment Adherence Program (TAP) is to improve medication adherence for patients being treated in CMHCs for severe and persistent illnesses. It is an enhancement of Missouri's implementation of CNS' BPM program. It consists of an early alert system when patients fail to refill essential prescriptions in a timely manner and as an educational resource for providers on best practices in improving treatment adherence.

Design

Missouri Medicaid patients who were prescribed at least one of nine orally-administered antipsychotic medications and who had at least one Medication Possession Ratio (MPR) score below 0.8 were included in the adherence intervention group. The MPR is a measure of the percentage of compliance derived from claims data that calculates to percentage of time without medications (i.e., days from a lapse of a prescription refill). The prescribing clinicians and case managers were messaged electronically two times per week at the point that failure to refill the targeted prescription was identified. Notification occurred when the prescription had lapsed at 7 days, 30 days, and 45 days, and occurred in real time. In addition, MPR scores were provided monthly for the most recent six-month period. MPR scores were calculated as the ratio of days of drug in the patient's possession divided by the days of drug prescribed by the clinician and were based on Medicaid claims data. Case managers received educational training sessions focused on antipsychotic prescribing, implications of medication side effects, reasons for medication discontinuation and key messages that case managers can share with their patients to motivate them to maintain treatment. Physicians received a concise brochure with current best practice guidelines on partial compliance, medication discontinuation, medication adherence tactics, patient motivation methods and an adherence algorithm that physicians may utilize during a prescription refill visit.

Development Timeline

It took one year to bring the project from initial concept to first intervention. Approximately four months each to develop the concept and obtain funding, develop data analytics and educational material, and finally recruit and train the initial sites.

Program Cost

Overall cost of the first year is approximately $250,000.

Measured Results

Change in MPR scores was measured for both the intervention group and a matched control group. Trends in MPR scores were analyzed for both groups pre-, during, and post-intervention.

Outcomes

During the pre-intervention period, the intervention group had a lower mean MPR score than the control group. In both the intervention and post-intervention periods, however, the MPR difference between the two groups was no longer statistically significant. The intervention group had a significantly greater increase in MPR score between pre-intervention and intervention periods. After the conclusion of the TAP intervention, the MPR score decreased somewhat but was still higher than the pre-intervention period. The change in MPR score in the intervention group is no longer statistically significant compared to the comparison group. For more information please contact the resource below.

Lessons Learned

Both case managers and psychiatrists were appreciative and found the reports and warnings useful. They reported that the intervention identified an actual previously unknown gap in care approximately half of the time. The remaining gaps were planned medication changes, delayed refill due to dosing changes, or use of samples to reduce co-pay obligations.

Promising Practice

This practice has only been implemented at one site (Missouri). However, its outcomes have been evaluated using a pre-post design with a control group and demonstrated statistically significant improvements in quality.

For More Information

Visit http://www.dmh.mo.gov/MHMPP/MHMPP.htm or e-mail Joe Parks at Joe.Parks@dmh.mo.gov.

Washington: Mental Health Law and Confidentiality Emerging Practice

Background

As part of a new emphasis on antipsychotics (AP) and mental health safety, Washington (WA) Medicaid developed a poly-pharmacy/poly-prescribing notification service. However, in 2006 it became apparent that State law precluded sharing of prescription information between prescribers of APs to a single client. The mental health confidentiality statutes and rules gave an AP prescription the same status as a mental health treatment record. Additionally, mental health diagnosis in the medical claims was thought to constitute a mental health treatment record. In consultation with the mental health division, attorneys general (AG), and Medicaid, a statute change was put forward as agency requested legislation.

Development Timeline

Three to four months of meetings and information sharing between Medicaid and Mental Health laid the groundwork for request of legislation in the fall before a January legislative session. Prior to the legislative session, Medicaid and Mental Health had numerous communications and conferencing with stakeholder groups explaining the safety issues involved in the potential of too many prescribers giving drugs to a single client without sharing the drug and rationale. Final legislation was posted and implemented in July of 2007.

Program Cost

No cost other than staff time, AG billings, and meeting time.

Measured Results

The agency obtained letters of support from the mental health community, advocates (e.g., the National Alliance on Mental Illness [NAMI]) and provider societies allowing the State to change the current statute.

Outcomes

The bill was passed allowing the sharing of prescription information and diagnosis.

Language From the New Law (SB5773)

Sec 1 2(m): For purposes of coordinating health care, the department may release without informed written consent of the patient, information acquired for billing and collection purposes as described in (b) of this subsection to all current treating providers of the patient with prescriptive authority who have written a prescription for the patient within the last twelve months. The department shall notify the patient that billing and collection information has been released to named providers, and provides the substance of the information released and the dates of such release. The department shall not release counseling, inpatient psychiatric hospitalization, or drug and alcohol treatment information without a signed, written release from the client.

Sec 2 (35): "Treatment records" include registration and all other records concerning persons who are receiving or who at any time have received services for mental illness, which are maintained by the department, by regional support networks and their staffs, and by treatment facilities. Treatment records include mental health information contained in a medical bill including but not limited to mental health drugs, a mental health diagnosis, provider name, and dates of service stemming from a medical service.

Lessons Learned

Groundwork should included examples of harm and potential client risk without good prescriber communication. Presenting these examples to the community helps to make for a common dialogue. Also, working closely with the Mental Health Department is crucial for a good outcome.

Emerging Practice

This new statute has not yet been challenged but it is only two years since its passage. It applies to all Medicaid clients and has very broad acceptance in the community.

For More Information

Visit: http://apps.leg.wa.gov/billinfo/Summary.aspx?bill=5773&year=2007 or e-mail Jeff Thompson at ThompJ@dshs.wa.gov.

Washington: Generics First Promising Practice

Background

The appropriate use of psychotropic medications in youth is an important public health concern. Several statutes have been enacted emphasizing the importance of evidence-based medicine (SB6088—PDL, HB1088—improving access to mental health treatments, and HB2575—health technology assessments). In 2009, the legislature passed SB5892 authorizing five tools for Medicaid to use to better control pharmacy costs and improve quality:

- Authorizing prescriber feedback reports using peer-to-peer statistical comparisons with removal of dispense as written (DAW) privileges with aberrant prescribing practices
- Introducing generic onto the PDL without P&T review
- Authorizing a generic first program for all new starts (mental health drugs and PDL drugs)
- Introducing over the counter (OTC) drugs onto the PDL without P&T review
- Introducing means to control off label use

Development Timeline

The statute and program was developed over approximately three to six months in discussions with the community. Implementation was approximately three to six months and included authorizing administrative codes and feedback reports. Generic first for antipsychotics in children was discussed in the community mental work group, the P&T/DUR and incorporated into the existing second opinion program.

Program Cost

The statute and policies were part of a savings package to improve generic performance from 62 percent generic fill rates to 82 percent. Each one percent represents a ~$4 million savings in the overall pharmacy program.

Measured Results

~350 AP second opinions have been conducted over the last year. At this time, we have not reviewed the AP second opinion program for reduction differentiating the dose and age from generic first (i.e., generic risperidone first) based on the agreed to criteria below.

Provider feedback reports were given to ~900 prescribers who had generic rates <80 percent, use of DAW >25 percent or who were statistically aberrant from peers (PCP, mental health, pediatrics and other). Prescriber were compared to other peers and best practices (top quartiles). Claims from the pharmacy system were used to monitor trends. Two newsletters and one set of reports were sent to prescribers. After providing 824 prescribers with their baseline measures in six therapeutic classes the following results were noted:

- One hundred and twelve prescribers (112) are now above 80 percent generic prescribing and below 25 percent DAW in six therapeutic classes
- Of the other 712 prescribers, for at least one therapeutic class:

- 29 percent improved both generic and DAW
- 54 percent improved generic only
- 45 percent improved DAW and
- 18 percent had no change

- The best practice group (top quartile): 47 percent improved both generic and DAW, 85 percent improved generic only, 49 percent improved DAW, and 13 percent had no change.
- One hundred and sixty (160) providers have moved up to best practice group.
- Comparing the best practice group to the peer group, there were no differences on average with long acting narcotics and as high as 185 percent better in ADHD drugs.
- In the provider peers, we noted an improvement of 21 percent in pediatrics, three percent in primary care, five percent in mental health and no change in other providers

Lessons Learned

A statewide second opinion process for generic new starts with mental health drugs is possible (AP, ADHD, and antidepressants). Using a community work group State providers, advocates and State officials can agree on generic programs. The following principles were agreed to:

The criteria for a brand rather than a new start are:

- Use of another brand name atypical antipsychotic is actually continuation therapy of what is a currently stable regimen.
- There has been a past trial of risperidone that resulted in discontinuation due to side effects.
- There has been a past trial of risperidone that resulted in discontinuation due to lack of benefits.
- There is a history of hyper-prolactinemia.
- When there are FDA indications not covered by risperidone or another generic.
- Exceptions are made through a peer-to-peer second opinion when a brand is requested.

Promising Practice

The policy and process was not only enacted into statute but had broad community agreement (Pediatric and Mental Health Associations, Mental Health Community Clinic Association and WA State Medical Association). Provider feedback reports appear to be effective in changing prescriber prescribing behaviors.

For More Information

E-mail Jeff Thompson at ThompJ@dshs.wa.gov

California: Medication Therapy Management Services (MTMS) Emerging Practice

Background

"Medication Therapy Management Services (MTMS) to Ensure Safe and Appropriate Use of Psychotropic Medications for Mental Health Patients in San Diego County: A Pilot" is a pilot program that has been developed by investigators at the University of California, San Diego (UCSD) in collaboration with CalMEND of the California Department of Health Care and San Diego County Mental Health Services. The pilot program site is a single outpatient clinic where clinical pharmacists trained in psychiatric pharmacy are an integral part of the multidisciplinary care team. The pharmacists provide direct patient care for chronic medication management under a Collaborative Practice Protocol. Pharmacists also provide drug information and education to patients and other providers at the clinic.

In the treatment of mental health care, it is often necessary to combine a full range of services, including psychosocial, pharmacotherapy and rehabilitative services. A multidisciplinary approach must be taken to provide effective care that is patient-centered and well coordinated. Mental health often co-exists with other medical conditions such as heart disease and diabetes; coordination of care that addresses these medical comorbidities is crucial for patients' overall health. MTMS utilizes highly trained psychiatric pharmacists to provide medication education and management.

Development Timeline

From conception to start date of the pilot program, the duration was 18 months.
Phase 1 of the development was conducted over a one-year time period beginning in the fall of 2007 and included:

1. Conducting literature review of MTMS best practices
2. Identifying a clinic site within San Diego County Mental Health Services
3. Integrating CalMEND initiatives into pilot project scope

Phase 2 of the development was initiated in early 2008 and is ongoing. It iincludes:

1. Developing a psychiatric MTMS program provided by pharmacists by:
   a. Designing MTMS based upon best practices and current literature
   b. Determining feasibility of integration into a county system based upon client, providers and clinic characteristics

Evaluating availability of clinical pharmacy expertise for implementation

1. Creating an experimental research for program evaluation:
   a. Exploring and document current data sources and collection practices in clinics.
   b. Exploring funding sources to support pilot program.
2. Developing a Collaborative Practice Protocol for psychiatric pharmacists to provide chronic medication management at UCSD Outpatient Psychiatric Services (clinic site).
3. Conducting a 12-month MTMS program at designated clinic site.
4. Evaluating by using the following data:
   a. Patient level data (pre-and post-intervention quality improvement indicators);
   b. Program level data (operations);

c. Clinic level data (e.g. feasibility, scheduling, staffing); and
d. Client satisfaction.

Funding Source

1. No CalMEND/DHCS funding resource was allocated for the pilot program. Once data is collected at the completion of the pilot, funding will be determined.
2. UCSD investigators have secured additional funding from external sources. Initial start-up and implementation is funded through in-kind contributions from UCSD.

Measured Results

The following hypothesis will be tested:

1. Increased proportion of patients will be adherent to laboratory monitoring orders after the MTMS intervention compared to proportion of patients before the MTMS intervention.
2. MTMS intervention will increase the number of patients seen for medication management at the county site.
3. Clients in the MTMS intervention group will be satisfied with the pharmacy-provided services.

Outcomes

Results will be available at the completion of pilot.

Lessons Learned

1. Funding for MTMS will remain a challenge. Our approach is to begin with a pilot study to collect data for evaluation, while continue to seek additional funding to support a large-scale demonstration project.
2. In fiscal year 2009, Veterans Health Affairs Mental Health Services is funding expansion of hiring clinical pharmacists and incorporating their roles in the care team. Providing MTMS to mental health care clients is becoming the standard and best practice.
3. Limitations in electronic medical record system can be challenging for data abstraction (for example, the absence of medication refill data at this particular pilot program site).
4. Reimbursement issues for pharmacists may limit the ability to generalize of the program.

For More Information

E-mail Penny Knapp at Penny.Knapp@dmh.ca.gov.

California: CalMEND Collaborative Performance Improvement Project Promising Practice

Background

CalMEND initiated the development of a Program Improvement Plan (PIP) in the fall of 2006 as a pilot with four county mental health services. The goal is to form a learning collaborative that brings together the stakeholders, including payers, providers, and consumers to study quality improvement. Participants meet monthly by conference calls and quarterly by in-person meetings.

The California External Quality Review Organization (EQRO) assisted the group in the development of a formal quality improvement plan that meets EQRO standards. The first study chosen by the learning collaborative was "Concurrent Use of Antipsychotics for Medi-Cal Beneficiaries."

Development Timeline

The pilot was initiated in fall of 2006. Baseline measurement collected in January 2007 includes statewide and county specific rates of poly-pharmacy. Each participating county developed specific interventions, which were approved by the county quality improvement team as well as EQRO. Each county began implementation of interventions in the fall of 2007. The pilot study time period is 18 months.

Program Cost

Each participating county is required to commit monetary resources to cover travel expenses for in person meetings by their county staff. The learning collaborative recommends a county team to have following members as representatives: quality improvement manager, medical/pharmacy director, data analysts and other QA staff or clinicians. There was also the cost of CalMEND consultant time for two years. Medi-Cal Pharmacy Benefits Division data analysis group staff time and pharmacy policy branch provided dedicated staff time as part of routine work with no extra cost.

Funding Source

The Mental Health Service Act (MHSA) funded CalMEND consultant time. County Mental Health Services funded the travel time and expenses for each county and Medi-Cal Pharmacy Benefits funded the staffing allocation.

Measured Results

The performance metrics include the rates of poly-pharmacy (as defined by the learning collaborative).

Measure an Effect Using Data Elements from the Data Dictionary

Data elements include demographic data (eligibility, age, gender, ethnicity, geographic location by county); prescribers (multiple prescriber per beneficiary, prescribing patterns, drug, dose, concurrent use of antipsychotics or poly-pharmacy), data on medication procession ratios or gap in prescription fills.

Trending data is available quarterly from July 2006 through current quarter ending September 2008. The rates of poly-pharmacy is holding steady.

Outcomes

Each of the four participating counties developed an individual intervention plan aimed at improving the use of antipsychotics, including reducing poly-pharmacy and improving adherence through client education in shared decision making. A full report was issued in 2009 and can be optained by contacting resource below.

Lessons Learned

- Learning collaborative that involves stakeholders with shared common interest helps to build consensus leading to more effective problem solving.
- The collective wisdom of the pilot group can be shared with others to facilitate rapid learning and spread.

For More Information

E-mail Penny Knapp at Penny.Knapp@dmh.ca.gov.

California: Stakeholders (Client & Family) Engagement in the Development and Implementation of CalMEND Clinically Informed Outcome Measurement
Emerging Practice

Background

CalMEND was established in 2005 as a quality improvement program to promote wellness and recovery for individuals with mental illness. Supported by funds from MHSA, CalMEND operates under the sponsorship of the Pharmacy Benefits Division of DHCS in collaboration with the California Department of Mental Health.

CalMEND's mission is to develop and support publicly funded mental health services and supports in California that are person-centered, safe, effective, efficient, timely and equitable, that are supported by friends and community, that promotes wellness/recovery, and that fully incorporate shared-decision making between consumers, family members and providers. CalMEND believes that client and family members must be an integral part of the development of services and supports to achieve success. All committees, subcommittees, and their work groups have client and family member participants who consistently provided input and influence in CalMEND projects, workgroups and collaborations. One example of the success of engaging client and family members into CalMEND is the development of the CalMEND Clinically Informed Outcomes Management (CIOM) system.

CIOM, a consumer self-report survey that provides feedback and recommendations to the treatment team to optimize care outcomes, was developed and implemented by Dr. Ann Doucette. To achieve these goals, CalMEND CIOM is designed as Web-based and provides real time feedback by electronically generating a report based on the client's input. Clients fill out the Web-based questionnaire at the clinic visit, and by eliminating turnaround time, clinicians, care takers and clients can monitor and adjust treatment using the client feedback before the end of the clinic session. Reports are retained for continuous assessment and monitoring throughout the length of the treatment.

Development Timeline

The first phase of the development was the design of CalMEND CIOM feedback form, which took nine months. The second phase was to make this form Web-based. This phase of development is ongoing and includes expanding the range of reports available for individual clients, providers, clinics, and agencies. There is a plan to develop translations into select languages. The third phase of the development is to pilot in clinics. The pilot will be in collaboration with Los Angeles County Department of Mental Health (LACDMH) and the Mental Health Alliance-Los Angeles (MHA-LA).

Program Cost

Funding for CalMEND consultants are from MHSA, other staffing support from the Department of Health Care Services and the Department of Mental Health

Measured Results

CIOM measures client feedback in the following modalities: symptoms, functioning, including physical health, co-occurring substance abuse, therapeutic alliance, and social support/connectedness and recovery, including recovery from substance abuse.

Outcomes

Not yet implemented; not available at this time.

Lessons Learned

- Client and family members are integral part of the team in the development of services and supports that are client-centered
- The essence of a person-centered approach—especially as compared to a program-centered approach—is that clients receive the services and supports that they want and need and are not simply matched with and provided a pre-determined menu or program of services.
- To effectively promote a client's recovery progress, a variable range of clinical services and service intensity will likely be required over time. The use of CIOM will continue to support development of future client-centered services and supports with recovery as goal.

For More Information

E-mail Penny Knapp at Penny.Knapp@dmh.ca.gov

Indiana: Mental Health Quality Advisory Committee Promising Practice

Background

During the 2005 Indiana General Assembly, the legislature passed the House Enrolled Act (HEA) 1325 and the Governor subsequently signed it into law. This model legislation essentially requires open access to mental health medications provided by managed care organizations (MCOs) operating in the Indiana Medicaid program. The Medicaid fee-for-service (FFS) plan had already been providing open access as a result of previous legislation.

The legislation created the Mental Health Quality Advisory Committee (MHQAC) to provide advice as to its implementation. Pursuant to the statute, the MHQAC is comprised of the Medicaid Director or their designee (who chairs the committee); the Medical Director of the Division of Mental Health and Addictions (DMHA), Family and Social Services Administration (FSSA); a representative of a statewide mental health advocacy organization; a representative of a statewide mental health provider organization; a representative from an MCO that participates in the State's Medicaid program; a member with expertise in psychiatric research representing an academic institution; and, a pharmacist licensed under Indiana law. The purpose of the committee is to develop guidelines and programs to allow open and appropriate access to mental health medications, educational materials to prescribers, and to promote appropriate use of mental health medications. All recommendations made by the MHQAC must be reviewed and approved by the Indiana Medicaid DUR Board prior to implementation. The DUR Board serves as an advisory body to the Office of Medicaid Policy and Planning (OMPP).

The committee and pharmacy staff from FFS and MCOs subsequently proposed and developed sophisticated, customized poly-pharmacy claim editing algorithms that were integrated into each of the respective claims processing systems. The initial set of edits were based on collective review of data and focused on outlier prescribing patterns. For purposes of this summary, the MHQAC activities have been listed below in the various phases of implementation.

Phase I: Initial Poly-Pharmacy Editing Algorithms

On January 1, 2007, six initial mental health quality edits were implemented in the pharmacy claims processing systems of both FFS and MCO plans. These edits, which when encountered by the dispensing pharmacy, will require a medical necessity review via the existing prior authorization systems, and apply to the following clinical situations:

- Patient receiving two or more tricyclic antidepressant medications
- Patient receiving two or more typical antipsychotic medications
- Patient receiving three or more atypical antipsychotic medications
- Patient receiving three or more antipsychotic medications
- Patient receiving three or more benzodiazepine medications
- Patient receiving three or more any antidepressant medications, excluding trazodone

Paid pharmacy claims from the most recent 45 days, where the days' supply is greater than 14 days, are reviewed during the editing process. Medications with identical ingredients but different salts (such as oral risperidone and injectable risperidone) were only counted one time for the purpose of counting medication experiences. Claims with days' supply of 14 days or less are excluded from the edits to allow for tapering. Customized pharmacy messaging was developed in order to communicate the nature of the edit to the dispensing pharmacy.

Phase II: Dose Optimization Editing

On June 19, 2007, the DUR Board and the MHQAC implemented dose optimization edits for mental health medications. These quantity per day limits were developed for all mental health medications and are reviewed quarterly for new drugs and clinical updates. The edits were developed to enhance quality and appropriateness in mental health prescribing practices. The edits were implemented consistently across the MCO and FFS programs. When a provider submits any claim that is not within the recommended edit criteria, the claim denies and is subject to the PA process.

Phase III: Additional Poly-pharmacy, Dosing and Trial Fill Edits

The following, additional quality edits were developed and approved by the DUR Board and the MHQAC. Implementation dates are listed where applicable. Certain edits have not yet been implemented due to claims processing limitations or anticipated high incidence of false positives.

- 15 day trial fill for new atypical antipsychotic medications (variable implementation dates)
- Patient receiving two or more sedative-hypnotics, including trazodone (March 3, 2008)
- Patient receiving two or more SSRI and/or serotonin–norepinephrine reuptake inhibitors (SNRI) antidepressants, excluding bupropion and mirtazapine (March 3, 2008)
- Patient receiving two or more stimulants having different core ingredients (TBD)
- Patient receiving three or more of any anticonvulsant/mood stabilizer (TBD)
- Patient receiving two or more atypical antipsychotics (TBD)
- Patient, ages 18-64, receiving the following low dose atypical antipsychotics:
  - aripiprazole < 10mg/day (TBD)
  - olanzapine < 5mg/day (TBD)
  - quetiapine < 300mg/day (TBD)
  - risperidone < 1mg/day (TBD)
  - ziprasidone < 40mg/day (TBD)
  - quetiapine: claims for 25 or 50 mg doses for patients ages 18-64 require PA; use for sleep induction is not an approvable diagnosis (March 3, 2008)

Phase IV: SmartPA Implementation for the FFS Medicaid Program

OMPP, through an optional service provision in the existing contract with ACS State Healthcare, is in the process of implementing SmartPA, a real-time solution comprised of highly sophisticated clinical PA rules that utilize integrated Indiana-specific evidence-based criteria. SmartPA uses clinical rule sets that incorporate member medical and pharmacy claims history to determine the appropriateness of the prescribed therapy. The solution will be implemented into the FFS pharmacy claims processing system and has clear advantages for assuring appropriate use of mental health drugs:

- Aggregates multiple pharmacy claims within each clinical rule to determine total daily dose and the existence of poly-pharmacy
- Utilizes medical claim information within the clinical rule to screen for procedure codes and/or appropriate diagnosis
- Prescribers can be included or excluded from the clinical editing and prior authorization requirements based on the National Provider Identifier (NPI) of the prescriber
- Automates 60-90 percent of prior authorization requests that would have traditionally required a phone call or completion of a prior authorization form

The implementation timeframe for SmartPA is scheduled for the fall of 2009. The following clinical rules are in development or are being revised from the previous approval/implementation:

- Patient receiving two or more SSRI and/or SNRI antidepressants, excluding bupropion and mirtazapine
- Patient receiving two or more stimulants
- Patient receiving three or more of any anticonvulsant/mood stabilizer
- Patient receiving two or more sedative-hypnotics, including trazodone
- Patient receiving two or more atypical antipsychotics
- Patient receiving two or more typical antipsychotics
- Patient 18 and over receiving the following low dose atypical antipsychotics:
  - aripiprazole < 10mg/day (TBD)
  - olanzapine < 5mg/day (TBD)
  - quetiapine < 300mg/day (TBD)
  - risperidone < 1mg/day (TBD)
  - ziprasidone < 40mg/day (TBD)
- OMPP is also evaluating the use of the SmartPA tool for ensuring adherence to the prescribed therapy. Adherence would be measured in real-time using the proportion of days covered methodology. Non-adherence thresholds would be established. When the allowable threshold is exceeded, one or more of the following interventions would be triggered:
  - Level 1: The dispensing pharmacist would be required to obtain PA
  - Level 2: A letter or phone call to the prescriber would be initiated
  - Level 3: The prescriber would be required to obtain PA

Development Timeline

Implementation dates for each of the respective edits are noted in the background section.

Program Cost

- Initial poly-pharmacy editing: $63,000 in FFS pharmacy claims processing systems changes. MCO costs are not available.
- SmartPA—one time implementation fee of $740,000, annual licensing fee $425,000
- What was the funding source? (e.g., Administrative, Medicaid State funds, other)
- State and Federal Medicaid funds, enhanced Federal match for SmartPA implementation obtained through the use of an Advanced Planning Document (APD)

Measured Results

A preliminary analysis was conducted comparing atypical poly-pharmacy trends before and after the implementation of the three or more APs edit. In the FFS Medicaid program, a 32 percent reduction in the use of two or more APs was experienced across the population.

Outcomes

- A comprehensive outcomes analysis has yet to be performed. An initial savings analysis for each MCO and the FFS program was conducted in January of 2008 and can be found at http://www.indianamedicaid.com/ihcp/PharmacyServices/MentalHealthInfo.asp?comm=qac.
- Significant savings were experienced with the implementation of dose optimization editing. Reductions in poly-pharmacy and associated expenditures were also experienced in certain therapeutic classes. It should be noted that, on average, prices for single-source brand drugs increased at a rate of eight to nine percent per year, which makes an accurate determination of savings difficult to ascertain. In addition, Indiana's best in class State Maximum Allowable Cost program (SMAC) for generic drugs was identified as a primary driver for a portion of the savings. Further information on the SMAC program can be found at: http://in.mslc.com/StateMacServices.aspx
- Consistent claims editing and prior authorization criteria across MCO and FFS programs.
- A preliminary analysis was conducted comparing atypical poly-pharmacy trends before and after the implementation of the three or more APs edit. In the FFS Medicaid program, a 32 percent reduction in the use of two or more atypical antipsychotics was experienced across the population.

Lessons Learned

- Consistent application of criteria and standards across all Medicaid benefit plans (FFS and MCO) is crucial for successful implementation and acceptance.
- If you could initiate the program again, what would you do differently? Clearly identify quality measures that could be utilized to measure the success of each implemented edit.

Promising Practice

The practice has consistency of criteria across all Medicaid benefit programs, use of customized claims editing technology and participation of all interested stakeholders. Practice is based upon reasonable evidence, is relatively mature, cost-effective, generally accepted by the provider community and has resulted in utilization shifts in the desired direction that do not appear to impact the quality of overall care. This is a promising practice because outcomes and comprehensive analysis have not yet been measured or performed.

For More Information

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Massachusetts: Working Group on Psychoactive Medication for Children
Emerging Practice

Background

The increase in the use of psychoactive medication in children, including prescriptions of antipsychotic medication, has led to public and government concern about the clinical and financial implications of these drugs. In response, the Massachusetts Department of Mental Health (MDMH) and the MassHealth Office of Clinical Affairs convened a Working Group on Psychoactive Medication for Children.

Development Timeline

In 2007, the Working Group, with representatives from Pharmacy and Clinical Services from all the managed care entities (MCEs) serving publically insured children in Massachusetts, was formed.

The Working Group defined problems in care including:

- Even in the absence of consensus guidelines, some providers have been outliers as to choice of agent and doses prescribed.
- Some providers have practiced in isolation, for instance, without the benefit of collateral data from other child-serving agencies.
- Some children have received interventions limited to pharmacotherapy, when comprehensive care was needed.
- Some providers have prescribed medication based on reports from only one source (parents) and one setting (home).

In meetings during 2008, the Working Group:

- Noted a lack of consensus as to the data needed to follow and manage trends in psychoactive medication use in children;
- Noted a lack of consensus as to how to monitor such care, both in the aggregate (quantitative) and on the individual level (clinical);
- Noted a lack of consensus as to how to support those providing care; and
- Decided to gather data from all members, convene clinical review teams within each MCE, and to share data and findings from clinical reviews.

The Group then identified the following objectives:

- To develop consensus as to the data needed to track patterns of use of psychoactive (PsA) medication for children and collect such data;
- To develop, for the MCEs to implement, procedures for within-plan surveys in the aggregate and for second-level (clinical) reviews of selected children; and
- To share findings with other members of the Working Group when conducting the surveys and reviews.

Program Cost

Participation time of members; data processing time within each MCE.

Measured Results

Quantitative data as to medication use; clinical data from clinical reviews of outliers.

Outcomes

Date is being gathered and will be shared when the review is completed.

Lessons Learned

That all MCEs, along with State Departments, want to respond more affirmatively to changing prescription practices.
That most providers identified as outliers are glad to be contacted by their MCEs.
It remains to be seen whether these strategies will affect practices throughout the State.

Emerging Practice

Engaging the clinical community in understanding aggragate data, changing policy and procedures, and building trust so that varaiations in care can be understood meets some but not all of the mature practices criteria. It is difficult to measure the effectiveness of this practice and therefore is classified as emerging.

For More Information

E-mail MaryEllen Foti at maryellen.foti@dmh.State.ma.us.

New York: PSYCKES, Clinic-Based Continuous Quality Improvement and Drug Utilization Review Promising Practice

Background

The New York OMH partnered with the Department of Health (DOH) to develop a clinic based drug utilization review program using continuous quality improvement (CQI) to improve prescribing practices. OMH adapted PSYCKES for the Medicaid population as a tool to support CQI-focused DUR activities first in mental health clinics and then more generally for all physician prescribers in the State. PSYCKES is a portfolio of Web-based tools that provides access to administrative data such as Medicaid claims. PSYCKES measures adherence to best practices at the State, region, county, provider, clinic/program, and prescriber levels. It also provides secure, HIPAA compliant access to client level claims data to support and improve clinical decisionmaking.

OMH had previously established a voluntary multi-year initiative with licensed mental health clinics where an increase of seven percent over the Medicaid base rate was tied to participation and performance in a Statewide quality improvement initiative.

Development Timeline

Year 1: Building Readiness (July 2007–June 2008)

- OMH is funded by DOH for a four year project to adapt and implement PSYCKES for the Medicaid population.
- Questionable psychotropic prescribing practices were established by a Scientific Advisory Committee of national experts who identified 79 potential quality targets.
- Two sets of quality indicators for youth and adults were developed as the focus of the year one DUR intervention: (1) poly-pharmacy, and (2) the use of antipsychotics with high/moderate risk for cardiometabolic abnormalities among individuals with existing cardiometabolic conditions (e.g. diabetes and hyperlipidemia).
- Built consensus for an integrated State and city CQI initiative, obtaining agreement on DUR focus, aligning goals and requirements, and developing an approach that used lessons learned from each government agency.
- Engaging stakeholders: worked with statewide provider coalitions and mental health advocacy organizations to educate them about the project goals.
- Adapted the PSYCKES platform for Medicaid data and developed policies, procedures and an interface for secure access.
- Signed a DOH-OMH Memorandum of Understanding for release of Medicaid data to treating clinics via PSYCKES.
- Developed an education and training program and materials including CQI Handbook, PSYCKES User Manual, CQI-PSCYKES training, public Web site, and Web-based CME for prescribers.

Year Two: Implementation

- Kick off for New York City was July 1, 2008, and January 1, 2009 for rest of the State.

- Provide mandatory CQI team training for participating clinics, and voluntary technical assistance Webinars.
- Implement PSYCKES security procedures and access in participating clinics.
- Monitor progress on project requirements (e.g., participation in training, PSYCKES access, change of practice) and provide outreach and technical assistance for programs that are falling behind.
- Develop additional DUR indicators for year three interventions.
- Further PSYCKES-Medicaid development, including: (1) additional DUR indicators, and (2) adapt for use by consumers allowing access by Medicaid enrollees to their own Medicaid claims data.

Program Cost

Project Director: One FTE psychiatrist
PSYCKES application development:

- $800,000 to develop PSYCKES-Medicaid application
- One FTE and reallocation of existing resources to support database and security management
- Scientific advisory meeting and consultation—$30,000
- Two FTE SAS programmers
- Implementation Team (345 clinics statewide)
- One FTE Implementation Director
- One FTE: Medical Field Officer—Clinical training and consultation, development of clinical materials, CME
- Two FTE implementation support staff for ongoing monitoring and communications with sites
- Trainings (materials, support, food)—$50,000 for 39 trainings
- QI consultants: Four retired State QI directors hired back part time, each assigned a region of the State

Measured Results

The measures used to evaluate the impact and success of the project include:

- Percentage of eligible clinics participating in the project
- Use of training and technical assistance: (1) participation and evaluation of CQI training by participants, (2) CME participation and post test, and (3) technical assistance Webinars attendance and participation
- Rates of use: number of DUR outliers flagged for review that have their records reviewed (assessed via PSYCKES use logs)
- Changes in prescribing practices in two focus areas
- Cost savings

Outcomes

- Participation rates: 92 percent of eligible mental health clinics are participating in the project (337 clinics statewide).

- CQI Training: 100 percent of participating providers attended CQI training with average training evaluation score of 3.5 on a four point scale (1-4).
- All clinics were able to complete the online PSYCKES security management process.
- Voluntary use of technical assistance resources included 21 Webinars that had 986 participants, 129 prescriber Web-based CMEs were completed, three psychiatric in-services, and one psychiatric consultation.
- Preliminary results from the first four month Interim reports (120 of 129 NYC clinics reporting):
  - Project selection: Polypharmacy Indicators (PPI) was selected by 76 (63 percent), Cardiometabolic Indicators (CMI) 40 (33 percent), both 4 (3 percent).
  - Clinical reviews and practice change: For PPI, 1,919 individuals met the criteria, 872 reviews were conducted, and of those 141 (16.1 percent) changed status. For CMI, 940 met criteria, 499 were reviewed, and of those 90 (18 percent) changed status.

Lessons Learned

The IT capacity of providers varies widely. At present, most community mental health centers in the State do not have electronic medical records (EMRs), nor do they use e-prescribing or other computer-based applications in routine practice. Mental health clinics face many challenges in implementing DUR including the limited role of the medical model; use of part-time psychiatrist staff that are not well integrated with other clinic staff and workflows; staffing shortages and over 30 percent staff turnover annually, with difficulty recruiting and retaining psychiatrists and other essential clinical staff. Despite these obstacles, providers can be engaged in a CQI project focused on improving prescribing practices. Preliminary results suggest the feasibility of conducting a large scale clinic based quality improvement initiative supported by Web-based data sharing.

Promising Practice

The project is less than one year old. Data are available for all participating clinics both through the interim reports and the PSYCKES application. Preliminary findings suggest improvements in quality and cost. It is a large-scale implementation, in 337 clinics this year. Acceptance is evidenced by high participation rates and increasing requests from providers from other treatment sectors for access.

For More Information

E-mail Molly Finnerty at COMDMTF@omh.State.ny.us.

Oregon: Psychotropic Medication Utilization Management Unclassified Practice

Background

In December of 2007, the Oregon Department of Human Services (DHS) convened the Medication Management Workgroup to assess psychotropic drug use by foster children and to make recommendations to DHS. The workgroup reported to the Oregon legislature in April of 2008. In September of 2008, DHS requested the Oregon DUR Board provide recommendations on drug use in the population (see: http://pharmacy.oregonstate.edu/drug_policy/pages/dur_board/reviews/articles/PedPsychReview.pdf).

HB3114 was introduced during the 2009 legislative session (http://www.leg.State.or.us/09reg/measpdf/hb3100.dir/hb3114.en.pdf). The legislation requires mental health assessments be done prior to issuance of a second psychotropic drug to a foster child. The legislation also requires an annual review of medications for all foster children under 6 years old on one psychotropic or any foster child on more than two psychotropics. The annual reviews will be conducted under the Medicaid Retro DUR program.

Development Timeline

This legislation is effective on July 1, 2010.

Program Cost

No fiscal impact assigned to the legislation.

Measured Results

Undefined at this time.

Outcomes

Undefined at this time. Specific feedback reports to prescribers will be generated by the RetroDUR Clinical Review Program, which compares prescribing patterns relative to peers and includes specific recommendations for change. The Behavioral Health Team of DHS Child Welfare will review outlier cases.

Unclassified Practice

This is an unclassified practice because the program is not yet in effect; there thus has been no assessment of cost; no measured results and no outcomes.

For More Information

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Texas: Psychotropic Medication Utilization Parameters Promising Practice

Background.

In September 2004, the State Office of the Inspector General released a report raising concerns about the use of psychotropic medications by foster children in Texas. By February 2005, the Health and Human Services Commission (HHSC), Department of Family and Protective Services (DFPS), and the Department of State Health Services (DSHS) released the Psychotropic Medication Utilization Parameters for Foster Children. Details can be found at: http://www.dshs.State.tx.us/mhprograms/psychotropicMedicationFosterChildren.shtm. The Parameters were distributed to physicians providing care to Medicaid recipients throughout the State of Texas. The State medical professional organizations also circulated the Parameters among their membership. They were distributed to Child Protective Service staff and residential childcare providers as well as medical consenters and judges. By the fall of 2005, CPS regional nurses were hired to conduct training of staff and communicate with prescribing physicians.

In June 2006, HHSC, DSHS, and DFPS released a report (http://www.hhs.State.tx.us/news/release/Analysis_062306.pdf) that showed that during the five months after release of the Parameters there was a 7 percent decrease in the number of children prescribed psychotropic medications and a 29 percent decrease in those receiving two or more psychotropic medications. Each year since has demonstrated continued improvements with compliance with the Parameters. Details can be found at: http://www.hhsc.State.tx.us/medicaid/OCC/Psychoactive_Medications.html.

Senate Bill 6 (2005 Legislature) called for all foster children to receive their medical and behavioral care under a Medicaid-managed healthcare program. That program began in April 2008 as Star Health (Superior HealthPlan Network), which requires the implementation of the Parameters by the network providers. An online Health Passport is also part of this project which includes demographic data, a record of immunizations, prescription data, and Medicaid encounter data including provider and diagnoses, and medication allergies). Any individual involved with a foster child's care can request a review of the psychotropic medication regimen by calling the Star Health Network service manager. If the child's regimen is outside of the Parameters, the Star Health medical director or other qualified child psychiatrist reviews the case and consults with the prescribing physician as needed to achieve appropriate care. Star Health also receives real time prescription data that indicates if a child's psychotropic medication regimen is outside the Parameters and this triggers a review of the case. Psychotropic Medication Utilization Review reports are then sent to the appropriate parties. Aggregate reports from Star Health regarding these reviews are still in development but will soon be available on a monthly basis.

Development Timeline

The Parameters were developed over a six-month period and were shown to have positive impact within a few months after release. The fuller implementation of formal reviews and monitoring by the Star Health Network has taken several years and is still in development.

Program Cost

No estimate available at this time.

Measured Results

We used Medicaid prescription data and medical provider billing data that included psychiatric diagnoses and medical specialty of the prescriber.

Outcomes

It appears that the prescribing patterns have improved over the last four years but we do not have formal outcomes regarding the behavioral health status of the foster children.

Lessons Learned

It appears to have been beneficial to address psychotropic prescribing patterns with the foster care population with whom the State has more authority and to ultimately coordinate this within a single managed care network. It also appears that affecting prescribing patterns with the foster population has had a positive effect for the general Medicaid population, as the same physicians tend to see patients in both groups.

Promising Practice

The Psychotropic Medication Utilization Parameters for Foster Children have been implemented statewide for over three years. Our data analyses have shown promising positive results with ongoing increases in appropriate medication practices. Once the initial workgroup had developed the Parameters, implementation was relatively straightforward, with the agencies involved implementing the policy on a statewide basis. The Parameters were distributed to existing providers and are also available via the Internet. Acceptance by providers has generally been very high. Data reporting and analysis has proceeded smoothly, once the initial decisions about definitions and methods were made, and have required minimal additional resources.

For More Information

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Alabama: Stakeholder Engagement/Management and Consensus Building Interventions Emerging Practice

Background

Alabama Medicaid has identified a multi-year pattern of steadily increasing utilization of atypical antipsychotics. This pattern is present in all age ranges, but we chose to focus our initial efforts on those of people less than 5 years of age. Our first steps involved data analysis to establish the features and extent of the prescribing patterns, which resulted in the noted utilization. Our pharmacy claims data for calendar year (CY) 2007 revealed 412 children less than 5 years of age who had a claim for an atypical antipsychotic. Based on these findings, we began to reach out to the various stakeholders in the State in order to both engage them in the issue and to help build consensus on next steps. The following groups have been integrated into the process:

- Department of Mental Health: The commissioner, medical director, pharmacist, and various administrative staff received a data presentation.
- Pharmacy and Therapeutics (P&T) Committee: The data was presented and the P&T committee recommended the formation of a task force that would bring back recommendations. P&T minutes from the meeting are posted on the Agency's public Web site.
- Positive Antipsychotic Management (PAM) Task Force: This task force was formed with multiple stakeholders including the Department of Mental Health, academic and private practice child psychiatrists, Blue Cross Blue Shield (by far the largest private insurer in the State), ALLKids (the S-CHIP program in the State), pharmacists, and the Alabama Chapter of the American Academy of Pediatrics.
- Child and Adolescent Psychiatric Institute: A presentation was made to this large consortium of pediatricians, child psychiatrists, and consumers from across the State. The group offered many useful suggestions.
- Directors of CMHCs: a presentation will be made to this statewide consortium of center directors who provide the highest volume of care to underserved groups.

Design

The PAM Task Force is the sentinel group for assimilating input from the other groups and making recommendations to our Pharmacy and Therapeutics Committee. The task force agreed upon the following strategy:

Beginning in May 2009, focused mailings to prescribers of children under age 18 years through the CNS program on any CNS-Quality Indicator (QI) related to antipsychotics. Beginning in June 2009, educational phone calls to prescribers of an antipsychotic (first or second generation) of children ages 0-4 years by a board-certified child psychiatrist through Prest/CNS. A semiannual re-analysis of prescribing patterns, starting December 2009.

Development Timeline

The initial presentation outside the agency was February 2008 and the outreach/involvement process is still underway. Implementation timeline of operational strategy with providers is described above.

Program Cost

Costs have largely been staff time, routine P&T review, and minimal travel expenses.

Measured Results

Measurement included a high level of engagement and the substantive contributions of suggestions, ideas, and resources by stakeholders.

Outcomes

Targeted outcomes are engendering stakeholder buy-in and minimizing resistance to the recommendations of the task force. At this point, buy-in has been good. Resistance to task force recommendations will have to be measured after they are implemented. Goals include education to providers resulting in appropriate utilization of antipsychotics in the pediatric population.

Lessons Learned

Stakeholders have helped to define some of the unique situations that exist around prescribing these medications, and there are unlabeled indications/target symptoms for the use of these medications, which are established in peer-reviewed literature.

Prescribing Data

Prescribing provider types included physicians, registered nurse practitioners, clinics, and primary care prescribing an AP for children 0-4 years of age.

Breakdown of Medical Chart Review

For classification purposes, recipients were considered to meet FDA indications if they had a documented FDA-approved diagnosis, regardless of age, even if the drug specifically notes adult only.

Recipients were considered to meet unlabeled diagnosis criteria and target symptom criteria if they had a documented diagnosis or target symptom that was not FDA approved, but was considered to be an appropriate off-label use, regardless of age, as supported by peer-reviewed literature.

Total that Met Criteria	173	42%
Total that Did Not Meet Criteria/No Records	239	58%
Total Recipients	412	100%

Emerging Practice

This practice is still in development and key elements have yet to be implemented. Targeted outcomes are presently limited to achieving stakeholder acceptance and participation. There are as yet no outcomes focused on member experience.

For More Information

E-mail Robert Moon at Robert.Moon@medicaid.alabama.gov.

California: Epocrates (Education/Marketing) Promising Practice

Background

Epocrates, Inc., a California company that develops clinical information and decision support tools, enables healthcare professionals to find reliable clinical information quickly and confidently. More than 500,000 healthcare professionals, including one in four U.S. physicians, use Epocrates' mobile and Web-based products to help them reduce medical errors, improve patient care and increase productivity. The company's clinical content is developed by physicians and pharmacists and is continuously updated to keep users informed and up to date.

In California, Medi-Cal Pharmacy Benefits Division seeks to maximize the efficiency in the prescribing aspect of care delivery system to the Medi-Cal population. The solution is to make the Medi-Cal and Aids Drug Assistance Program (ADAP) contract drug lists (CDLs) available at the point of care for easy access to clinicians. Since the launching of CDLs in January 2007, more than 19,167 clinicains, including 6,102 physicians have loaded Epocrates Medi-Cal and ADAP drug formularies in a portable electronic format. As a result, prescribing physicians have the ability to see all available drug alternatives and restrictions on drugs, and more appropriately prescribe a CDL drug.

Development Timeline

Once the contract was in place, it took about four weeks to load the Medi-Cal and ADAP contract drug lists (CDL) used by pharmacists and pharmacy technicians into an Epocrates Web-based tool. Pharmacy staff does ongoing weekly updates.

Program Cost

The funding source is general funds from the Department of General Services. The fees and terms are confidential.

Measured Results

Utilization of California CDLs by Epocrates prescribers is indirectly measured using quarterly data on:

- The number of total clinicians as well as the number of MDs who have downloaded the Medi-Cal and ADAP CDLs.
- The number of drug lookups by MDs.

Outcomes

DHS California has not performed a retrospective study on the cost savings and ROI in the Epocrates solution for provider access to our CDLs. However, Epocrates presented DHS CA with studies other commercial health plans have completed. In one such study, there was an average of 0.9 percent increase in generic utilization resulting in a savings of $250,000 per one million members. In a different study, Epocrates physicians had lower Tier 3 rates (0.50 percent lower) and higher Tier 2 rates (0.57 percent higher) than a reference group of physicians.

Lessons Learned

- A multi-prong approach in announcing the launch of Medi-Cal contract drug list with Epocrates is essential to ensure maximum dissemination of information. Providing ongoing good customer services and support is critical in maintaining good utilization rates.
- Knowing whom our target audience and users helps us to prepare "Doc Alerts" that meet their needs.

Epocrates offers other services in which California did not consider participating. In the future, we may consider working with Epocrates on mobile CME programs. Epocrates also offers a platform for providing other tools such as guidelines, calculators, and risk assessments. We may consider using this platform to publish our guidelines in the future.

For More Information

E-mail Penny Knapp at Penny.Knapp@dmh.ca.gov.

Colorado: Medicaid Rx Review Program
Unclassified Practice

Background

The Rx Review Program is a statewide program that provides for one medication therapy counseling session per year between a contracting pharmacist and a Medicaid client. Pharmacists provide a comprehensive medication evaluation, which includes a review of all prescription medications as well as over-the-counter and nutritional supplements, to identify drug-drug interactions, drug-over the counter/supplement interactions, drug duplication, or use of multiple providers, if any.

Design

The Medicaid Department creates a client profile based on claims data listing the client's medications, providers, dispensing pharmacies and disease States. The client profile is sent to the pharmacist assigned to perform the consultation. Pharmacists must conduct the medication therapy counseling session in person unless the client cannot meet, then it can be conducted over the phone. Client selection used several factors including high drug utilization (taking at least five medications), disease states, and geographic proximity to contracting pharmacists. Participation in the program is voluntary so clients may decline the service. Once the session has been completed, the pharmacist must draft a letter documenting the meeting and any relevant recommendations. The pharmacist will send the letter to the Department, client, and the client's providers.

The program was created pursuant to State legislation. The authors of the bill were the primary drivers of the legislation, with the Wyoming PharmAssist program acting as a model.

Development Timeline

The program required federal approval via submission of a State Plan Amendment (SPA) and the publishing of a public notice of the reimbursement methodology. It took about nine months to draft, submit, and receive federal approval for the SPA. During that time, staff drafted pharmacist orientation materials and a standard letter for clients (two weeks) and a contract template for participating pharmacists (one month), and the Department performed outreach with several organizations/associations in order to recruit pharmacists. Staff estimate it will take about two weeks to perform a data pull that identifies potential clients. A statewide contract freeze became effective in October 2008, putting the program temporarily on hold. Staff determined in November 2008 that the contracts with participating pharmacists are exempt from the freeze; therefore we are proceeding with the final stages of implementation.

Program Cost

The program pays pharmacists $75 per medication therapy counseling session. The State legislation appropriated total funds of $16,950 for the pharmacist payments, at a fund split of 25

percent State and 75 percent Federal. The legislation also provided approximately $68,000 for one FTE to oversee the program, at a fund split of 50/50.

Measured Results

The specific metrics are under development, but generally the program will be reviewed to determine how effectively it improves client health outcomes, enhances medication safety, and reduces total health expenditures.

Outcomes

Not determined at this time; the program is in the final stages of implementation.

Unclassified Practice

The Rx Review program is not mature and outcomes, including cost effectiveness, improved quality, or improved access, have yet to be measured. A significant barrier to implementation was SPA approval.

For More Information

E-mail Kimberly Eggert at kimberly.eggert@State.co.us

Massachusetts: Public Education
Emerging Practice

Background

Parents and guardians, including social workers in the Department of Social Services (now, the Department of Children and Families) wanted information to help those who authorize children's medical treatments to make responsible, informed decisions regarding psychoactive medications. The Department of Mental Health convened a working group to address this need.

A document was produced and is available in English and Spanish online at the Department of Mental Health (DMH) public Web site:
http://www.mass.gov/Eeohhs2/docs/dmh/publications/psychoactive_booklet.pdf.

The document provides parents, guardians and others with information about psychoactive medications in children. It goes beyond the provision of information to help readers understand how children's emotional and behavioral problems are assessed, what are the elements of comprehensive care, and what criteria should be used in deciding to initiate or continue a trial of medication treatment.

Development Timeline

In 2001, a working group was convened representing interested parties in both the public and private sectors to produce a document. That document, "Psychoactive Medication for Children and Adolescents: Orientation for Parents, Guardians, and Others," was first made available in February 2002 and has since been revised three times, most recently in September 2007.

Program Cost

The time of those who developed the document and the costs of posting it on the Web site of the Department of Mental Health.

Measured Results

Satisfaction data are gathered informally from DCF social workers and supervisors.

Outcomes

DCF social workers report that the document is helpful.

Lessons Learned

Information needs regarding psychoactive medications for children can be met with a specially developed, Web-available document.

Emerging Practice

This intervention has yet to measure effectiveness.

For More Information

E-mail MaryEllen Foti at maryellen.foti@dmh.State.ma.us

Missouri: Road Shows for Behavioral Pharmacy Management (BPM) Emerging Practice

Background

As part of Missouri's implementation of Comprehensive NeuroSciences' (CNS) Behavioral Pharmacy Management (BPM) program, a series of meetings were held that were designed to inform prescribers and other stakeholders of the program and to answer questions and address concerns.

Design

Initially, these were primarily informational in nature, and consisted of grand rounds at various universities and medical schools in Missouri, CME presentations at annual meetings of Missouri behavioral health organizations, presentations to the professional staff at community mental health centers, and community invitational professional luncheons and dinners. The focus was to introduce the program to physicians and generate interest. We also utilize a Stakeholder Advisory Group composed of a diverse selection of Missouri behavioral health opinion leaders and advocates reviewing cost and quality data, and soliciting feedback on opportunities for improvement. Plans for pilot programs are unveiled, and data from such programs in progress are presented and reviewed. Generally lasting five to six hours and including a meal, these meetings are held in a central location and attract stakeholders from across the State. During implementation this group met every six months more recently it has met every 12 to 18 months.

Development Timeline

The initial introductory presentations took four hours to develop. Logistics for each event took approximately another four hours of staff time. The intensive introductory phase occurred over the first year of the project.

Program Cost

Overall cost of the introductory first year is approximately $10,000 specific to the project budget. This does not include any overhead from annual meetings that were already scheduled where we were one of several presentations and dinner meetings that we were invited to present at sponsored by local psychiatric societies.

Measured Results

On standard CME participant feedback forms these presentations were rated highly. Initially we received many letters, phone calls, and personal verbal contacts of individuals and organizations expressing their concerns that the intervention would be inappropriate or have negative impacts. We have not received any such communications for the past two years.

Outcomes

The significant outcomes were decreased resistance and community anxiety during implementation, increased understanding of the key principles making prescribing more

consistent with evidence-based practice, maintaining position/patient autonomy in making medication decisions, and focusing on improving quality first with cost control as a secondary outcome.

Lessons Learned

Attendance at road shows is highest when psychiatrists and other stakeholders are anxious and fearful regarding a new intervention and drops off significantly once the intervention is understood and accepted. Multiple exposures to a road show presentation appeared to be more effective than single exposures.

Emerging Practice

This practice is limited to one site (Missouri) and its outcomes data are limited to participant feedback without a control group. It is a time-limited startup/implementation practice. Its strengths include low-cost, high acceptance, straightforward implementation and favorable outcome based on available data. **For**

More Information

http://www.dmh.mo.gov/MHMPP/MHMPP.htm
E-mail Joe Parks at Joe.Parks@dmh.mo.gov

Missouri: Access to Consultation in Behavioral Pharmacy Management (BPM) Initiative
Mature Practice

Background

Behavioral Pharmacy Management (BPM) analyzes pharmacy-prescribing patterns and then mails a letter to individual prescribers making recommendations on how they can improve the quality of their prescribing practice involving psychiatric medications. Some prescribers receiving the letter have additional questions regarding the recommendations and how they apply to their individual patients. Consultants with expertise in psychopharmacology need to be available to answer their questions.

Design

The mailed intervention offers consultation with a psychiatrist specializing in psychopharmacology upon request. Consultation also occurs as outreach (cold call) to 20-30 prescribers monthly with the highest portion of potentially questionable prescription patterns. Initially, in 2004-2006, three local Missouri psychiatrists noted for expertise in psychopharmacology provided this service. These peer consultation phone calls tended to resemble a true "case consultation" format, and focused on specific patients, often in a series of multiple phone calls. In an effort to move toward a broader format focusing more on prescribing practices more generally rather than on specific challenging patients, and to avoid the large amounts of time that the local psychiatrists were spending to schedule these calls, Prest & Associates was brought in to handle the peer consultation calls in 2006.

Development Timeline

The initial approach using local psychiatrists took approximately three months to develop and implement. The current approach of contracting took approximately two months to plan and procure.

Program Cost

The initial cost of using local psychiatrists and the Prest & Associates contract was approximately $10,000 annually.

Measured Results

Prest & Associates delivers monthly reports on the number of physicians contacted, the number of completed consultations, and the number of physicians contacted without success.

Outcomes

There was increased acceptance of the intervention due to availability of consultation by psychiatrists as opposed to pharmacists. Some physicians who did not change their practice in response to the mailed message have changed in response to the consultant contact.

Lessons Learned

Anecdotally, it appears that non-psychiatric prescribers are more receptive to feedback and consultation regarding prescribing of behavioral medications than are psychiatrists, and are more likely express a willingness to change prescribing practices. Nevertheless, there is some indication that even outlier prescribers who protest that all of their outlier prescribing is clinically warranted do eventually make changes to their prescribing to bring it more in line with best practices. This would reinforce the value of repeated messaging via monthly reports and periodic peer consultation calls.

Mature Practice

BPM, including the consultation component, has been implemented in multiple States and received several awards as an innovative practice improving the quality of prescribing.

For More Information

Visit: http://www.dmh.mo.gov/MHMPP/MHMPP.htm or e-mail Joe Parks at Joe.Parks@dmh.mo.gov

Washington: Evidence-Based Mental Health Care Treatments Mature and Promising Practices

Background

A common theme is that a combination of medical treatment and social/behavioral care often ensures the best of outcomes. Unfortunately, tracking mental health treatments and associated medication use is made difficult by the lack of codes. Washington State has recommended a set of evidence based mental health treatments for the treatment of child and adolescent disorders.[1-6]

Design

The importance of engaging both a child and family in treatment cannot be underestimated. Several evidence based mental health treatment can be classified as mature and promising and are described below.

Development Timeline

Many if not most of these interventions are being used actively in practice. Unfortunately the integrity, adherence and outcomes are not tracked. Ensuring the fidelity of these evidence-based practices can be immediately implemented if incorporated into ongoing education programs, CME and monitoring services.

Program Cost

Each mental health treatment will have differing training and resource costs. Brief descriptions can be found at http://depts.washington.edu/pbhjp/.

Measured Results

Each mental health treatment will have differing measures and outcomes. Brief descriptions can be found at http://depts.washington.edu/pbhjp/.

Lessons Learned

Brief learning descriptions of each treatment can be found at http://depts.washington.edu/pbhjp/.

Mature Practices

- Dialectical Behavior Therapy addresses issues specific to individuals with borderline personality disorder. Information available at http://www.behavioraltech.org or http://www.brtc.psych.washington.edu/.
- Motivational Enhancement Therapy is a systematic intervention based designed to evoke rapid, internally generated changes in behaviors of abusers of drugs and alcohol. Information available at http://motivationalinterview.org.
- Motivational Interviewing has been expanded to address a variety of substance abuse issues as well as health promotion and medical treatment adherence. Information available at: http://www.motivationalinterview.org.

- Trauma Focused Cognitive Behavioral Therapy treats victims of sexual abuse and their non-abusive parents and since been expanded to treat other traumatic events in a child's life. Information available at: http://tfcbt.musc.edu/.
- Positive Parenting Program (Triple P) helping parents become self-sufficient in managing problem behaviors in their children improve family relationships and promote child social development. Information available at: http://www.triplep-america.com
- Parent Child Interaction Therapy to improve parenting behaviors through play therapies. Information found at: http://pcit.phhp.ufl.edu/
- Multisystemic Therapy services serious juvenile offenders and is designed to improve behaviors and outcomes. Information available at: www.mstservices.com.
- Aggression Replacement Therapy is a multimodal psychoeducational intervention designed to alter the behavior of chronically aggressive adolescents and young children. Information available at: http://artgang0.tripod.com/.
- Functional Family Therapy serves a population of at-risk adolescents and families become more adaptable and productive. Information available at: www.fftinc.com
- The Incredible Years strengthens young children's social competence and problem-solving abilities, and reduce aggression at home and school. Information available at: http://www.incredibleyears.com/
- Multidimensional Treatment Foster Care is a behavioral treatment alternative to residential placement for adolescents with chronic antisocial behavior, emotional disturbance, and delinquency. Information available at: http://www.mtfc.com/.
- Cognitive Behavioral Therapy is a framework to treat depression. Information available at: http://nacbt.org or http://www.beckinstitute.org/.

Promising Practice

- Relapse Prevention Therapy (RP) is a cognitive behavioral approach to helping the individual avoid backsliding or worsening of behaviors related to substance use. Information available by e-mail at gparks@u.washington.edu
- Family Integrated Transitions combines Multisystemic Therapy, Dialectical Behavior Therapy, Motivational Enhancement Therapy, and Relapse Prevention techniques to meet the unique needs of these youth and their families. Information available at http://depts.washington.edu/pbhjp/projects/fit.php.

References

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6. Provider Access Line: Updated 2010, http://www.palforkids.org/resources/. Accessed June 2010.

For More Information

E-mail Jeff Thompson at ThompJ@dshs.wa.gov

California: Relationship of Poly-Pharmacy Rate to Practice Setting Emerging Practice

Background

One percent (50 prescribers) of California's 5,000 Medicaid pharmacy providers account for over 30 percent of the clients receiving multiple atypical antipsychotics concurrently. There is little evidence to support this practice, which is generally referred to as "poly-pharmacy." Further analysis of this data showed that many of these pharmacies were "closed door" operations, serving mostly long term care facilities and/or assisted living facilities. Federal regulations governing the operation of long-term care facilities require that a pharmacist perform drug regimen review of all residents in skilled nursing facilities at least monthly. Any irregularities must be reported to the facility's attending physician and director of nursing, and these reports must be acted upon. This review is supposed to include an assessment of the presence of any unnecessary drugs, which would include multiple atypical antipsychotics.

Since the Licensing and Certification Division of California's Department of Public Health has responsibility for monitoring compliance (and the authority to enforce compliance) with these regulations, the Department of Health Care Services is collaborating with this sister agency to promote responsible prescribing and dispensing behaviors in facilities with high rates of atypical antipsychotic poly-pharmacy.

Development Timeline

It took one year, from conception to program implementation, to begin this collaboration.

Program Cost

There were no direct costs associated with collaboration, but a significant amount of staff time was required to develop appropriate AP poly-pharmacy metrics and agreements.

Measured Results

- AP poly-pharmacy rate among skilled nursing facility residents (pre- and post-review)
- Dollars recovered from pharmacy (If referred to audit and Investigation)

Outcomes

Results are forthcoming, but we anticipate a reduced AP poly-pharmacy rate per SNF facility, fewer claims per client, and reduced payment to pharmacies per beneficiary per month.

Lessons Learned

Collaboration with existing State programs can leverage existing resources and/or data and minimize the need for new programs that are redundant in function and purpose.

For More Information

E-mail Penny Knapp at Penny.Knapp@dmh.ca.gov.

California: Improving the Use of Antipsychotics: A Pharmacy Tool Kit for Measurement and Feedback
Emerging Practice

Background

As we began the study of antipsychotics utilization as a pilot collaborative performance improvement project (PIP) with four participating California county mental health services in California, it becomes apparent to us that we have accumulated significant knowledge and experience working with Medi-Cal claims and administrative data. Subsequently we developed a pharmacy tool kit with the goal of disseminating our lessons learned to the rest of the 54 counties in California. The pharmacy tool kit consists of (1) an overview of quality improvement methodology and concepts; (2) sample forms, tables, templates, sample reports, reference materials, clinical guides, pharmacotherapy literature review and summaries, and other helpful references; (3) a set of established quality measures in report format, based on Medi-Cal claims and administrative data; and (4) HIPPA compliance and protection of private health information (PHI).

The pharmacy tool kit supports quality improvement efforts and enables users to:

- Evaluate "best practices" for effective and efficient use of antipsychotics.
- Address over or under utilization of antipsychotics and to reduce unexplained variances.
- Gain further insights in the prescribing patterns.
- Identify areas of service needs based on demographic data, stratified by ethnicity, age, gender, and location.
- Access baseline data and ongoing measurements for tracking and trending of improvements, benchmarking to similar county by geographical location, population size and services.

Development Timeline

The development of the tool kit took 12 months, from January to December 2007. The vetting and review process is ongoing.

Program Cost

Not yet implemented.

Funding Source

Primary support: Medi-Cal Pharmacy Benefits Division.

Measured Results

A set of measures on prescribing patterns, including (1) poly-pharmacy (two or more concurrent use of antipsychotics, (2) out of range dosages (high/low), and (3) medication procession ratio (MPR) to measure adherence and/or gaps in therapy.

Measure an Effect Using Data Elements from the Data Dictionary

Pharmacy and administrative claims: provider/prescribing information, dosage, day's supply, duration/gaps in therapy, concurrent use of antipsychotics, and demographic data.

Outcomes

Not available at this point.

Lessons Learned

Developing measurements that are well tested for reliability and feasibility takes time and effort— "If it is not measured, it cannot be improved." State Medicaid programs are best positioned to carry out initiatives like this, which requires significant initial start up time and efforts. A tool kit provides potential users "turn key" resources to jump-start a quality improvement program and significantly reduces barriers due time and resource constraints.

For More Information

E-mail Penny Knapp at Penny.Knapp@dmh.ca.gov.

Colorado: Comprehensive NeuroScience (CNS) Promising Practice

Background

Starting June 1, 2006, the Department engaged in a two-year project with Comprehensive NeuroScience (CNS) to run the Behavioral Pharmacy Educational (BPE) program. Through this program, the Department was able to provide information to prescribers about the psychiatric utilization of their patients.

During the two-year span of the BPE program, educational alerts/letters were sent to prescribers to inform them if the medication dosing for their patients were in line with Food and Drug Administration (FDA) guidelines and, for children, research and consensus-based guidelines. The messages were advisory and intended to be supportive. Prescribers were asked to review each case in the context of the guidelines and decide individually what was best for the patient. The program was also designed to notify prescribers about forgotten refills and when a patient obtained the same class of drug from multiple prescribers. If prescribing patterns did not change, follow-up letters were sent to the prescribers. When deemed necessary, peer consultants met with prescribers to discuss their prescribing habits and current clinical information regarding the drugs.

The program targeted the top 300 prescribers who had written prescriptions that deviated from best practices guidelines.

The Department supplied summary reports to our Behavioral Health Organizations (BHOs), which the clinics and prescribers found useful for internal quality improvement.

Development Timeline

Since contracts were needed between the Department, CNS and Eli Lilly, the sponsor of CNS, it was approximately one year from the time the Department decided to implement the program until the program started.

Program Cost

The program costs approximately $750,000 per year; however, this program was funded entirely by Eli Lilly, Inc.

Measured Results

While it was not possible to fully quantify health care outcomes, the program provided cost savings.

Outcomes

CNS was able to provide the cost avoidance information to the Department. CNS determined that the total cost avoidance for FY 2006-07 was estimated at $800,000 for adults and $1.1 million for children. This measure takes in account the full twelve months of the intervention in addition to the results that were observed in FY 2007-08 on the population that was intervened in FY 2007. The total cost avoidance for FY 2007-08 was estimated at $20,000 for adults and $20,000 for children. The FY 2007-08 results were based on data from three mailing periods for both adult and child populations and followed through the end of the program. There was a 49 percent reduction in adults and 64 percent reduction in children.

Lessons Learned

If the Department had paid for the program offered by CNS, it would have been cost neutral for the first two years. This program did not have the ability to offer continued cost savings after the initial two years. The Department also learned that mailings are not always an effective form of communication for the State of Colorado since our client and provider files are not accurate.

Promising Practice

This two-year program improved shifts in provider prescribing habits. The program had significant community acceptance as evidenced through provider surveys and outreach with stakeholders. Outcomes measures were reported by CNS and appear to offer some cost effectiveness for the first year. The second year of the program did not have the ability to offer continued cost savings. Overall, the program was considered cost neutral if the Department had paid for the program.

For More Information

E-mail Kimberly Eggert at kimberly.eggert@State.co.us

Maine: Academic Detailing
Maine Independent Clinical Information Service (MICIS)
Emerging Practice

Background

Academic detailing is an outreach educational program wherein trained clinicians make office visits to provide physicians with evidence-based information on how best to treat specific medical conditions. The program, which was first instituted in 2005 by the State of Pennsylvania's Pharmaceutical Assistance Contract for the Elderly (PACE) program in collaboration with Harvard University Independent Drug Information Services, emulates the highly successful drug company practice of sending detailers to doctors' offices to influence prescribing practices, with the goal of providing unbiased information so that clinicians will better align prescribing practice with current scientific evidence. As of mid 2009, nine States have undertaken academic detailing programs directed at prescribing practices in Type 2 diabetes, antibiotics for respiratory disease, pain relievers, cholesterol lowering drugs, pain relievers, anti-platelet drugs and mental health drugs.

The Maine legislature authorized the Maine Department of Health and Human Services Office of Medicaid Services to create an academic detailing program—Maine Independent Clinical Information Service (MiCiS). MiCiS,is based on the Pennsylvania PACE program, has two physician assistant academic detailers trained by the Harvard group that worked on the creation of the PACE, with materials purchased from PACE. Their first detailing topic concerned the initiation of insulin for Type 2 diabetes, the evidence for use of multiple oral agents, and the role of diabetes education in management. A second topic concerned antiplatelet agents: when, which one, how much. Participation has been voluntary. Prescribing data for MaineCare members is shared with the provider to show them how their prescribing habits compare to their peers. Partners in MiCiS are Maine Medicaid, Maine Medical Association, which recruited the academic detailers and provides educational materials, and GHS, the State's Medicaid pharmacy contractor, which supplies data analysis and clinical support. An advisory committee, which meets quarterly and has representatives from advocate groups, universities, providers, pharmacies, the two academic detailers, and Maine Medicaid, provides oversight.

An initial discussion with the advisory committee was held in April 2010 to launch a similar project to disseminate best practice guidelines for prescribing atypical antipsychotics. It is expected that medical staff from the State mental health authority, GHS and Medicaid, in collaboration with the State's Psych Work Group, will use national sources to identify best practice guidelines, with final selection of guidelines for appropriate prescribing and monitoring in the fall of 2010. The Psych Work Group is the equivalent in Maine of a P&T Committee specific to psychotropic medications and is composed of consumer advocates, community psychiatrists, representatives of professional societies and DHHS medical directors. Following selection of guidelines, training will be provided to the detailers who will be doing the academic detailing at provider sites. GHS is now collecting data on prescribing patterns and metabolic monitoring, which will be shared with prescribers who participate in this project.

Development Timeline

Planning for the Maine diabetes academic detailing project began in 2008. Training of the academic detail staff was completed in October 2008. Recruitment and office visits that educational material were implemented in February 2009 and are ongoing as of provide May 2010.

Program Cost

Maine Medicaid has funded the project through fees collected from pharmaceutical companies as a cost of doing business in Maine, in accordance with State law governing clinical drug trials. The cost of the first full year of the program was $218,400. Manufactures are required by law to submit a fee and report clinical trials. The MiCiS has completed a grant request to expand academic detailing, both within Maine and in a cooperative program with New Hampshire.

Measured Results

While there are several new State programs targeting antipsychotic medications, no results specific to antipsychotics are yet available. Evaluation of Maine's academic detailing project on diabetes and anti-platelet drugs has shown a high degree of satisfaction and acceptance by prescribers.

Outcomes

Data on changes to prescribing patterns has generally shown positive results. Acceptance has generally been good. Cost savings have also been demonstrated in many instances. Data related to antipsychotics is not yet available.

Emerging Practice

Academic detailing has been shown in multiple settings to be a promising practice for increasing prescribing according to evidence-based guidelines, with high levels of prescriber satisfaction. Idaho, Oregon, and South Carolina have instituted academic detailing projects specific to APs, but these programs are still in their first year and Maine's academic detailing program for antipsychotics is not expected to be implemented until 2011. While there is no specific reason that the experience with antipsychotic academic detailing will be different from the experience with other drugs, this is probably best described as an emerging practice at this time.

For More Information

Independent Drug and Information Service Web site: www.rxfacts.org/
Prescription Policy Choices: www.policychoices.org
Prescription Policy Choices Academic Detailing Toolkit:
www.policychoices.org/AcademicDetailingToolkit_000.shtml
Drug Effectiveness Review Project: www.ohsu.edu/ohsuedu/research/policycenter/DERP/
Community Catalyst: The Pew Prescription Project: www.prescriptionproject.org/
Maine Academic Detailing: www.academicdetailing@mainemed.com

Maine: Report Cards
Emerging Practice

Background

Antidepressant Adherence: MaineCare informs prescribers about their patients' failure to refill antidepressant medication prescriptions. Electronically submitted statewide pharmacy claims data is monitored weekly by Goold Health Services (GHS), the State's pharmacy management contractor. Any prescription for an antidepressant that is not refilled within 7-14 days is flagged and an automatic fax is sent to the prescriber. This project was launched in January 2006. On average, 2,899 letters are sent out per quarter.

Report Card: GHS sends quarterly reports to each prescriber who has a minimum of 20 Medicaid patients, documenting compliance with the preferred drug list (PDL) for all classes of drugs. These reports include per prescriber, the number of prescriptions and average cost for both preferred and non-preferred drugs in all major drug categories, including psychotropic drugs. There is no comparative data, however, allowing the prescriber to evaluate utilization in comparison to others.

Periodically, reports are generated on older patients and sent to each prescriber statistically comparing them to a peer (Z scores) to show how far off the prescriber is from the ideal.

Development Timeline

Undetermined.

Outcomes

Undetermined.

Lessons Learned

Medication therapy is effective for a wide variety of conditions and lack of medication adherence is an increasingly recognized problem. Prescribers are generally not aware of their patients' compliance with medication therapy.

Measured Results

Evaluation of the effectiveness of this approach is underway with results expected sometime in 2010 and can be obtained from the source below.

Emerging Practice

We consider these emerging practices. The comparative AP drug use study shows that Maine's rate of non-adherent use of AP drugs is almost 7 percent lower than the median of the 15 States studied, and has decreased 0.7 percent between 2004 and 2007. A variety of mechanisms are in use to increase medication adherence. Report cards, non-refill reminders, and reports of possible drug side effects are relatively low-cost and non-intrusive methods of providing prescribers of

information about patient medication compliance. We are not aware of studies showing the efficacy of these methods and are hopeful that our effectiveness evaluation will add to the knowledge on the subject.

For More Information

E-mail Elsie Freeman at Elsie.Freeman@maine.gov.

Massachusetts: Access To Consultation—MCPAP Mature Practice

Background

It is widely recognized that the need for child psychiatrists' services exceeds the supply nationwide. Nationally it is estimated that there are 1.6 child and adolescent psychiatrists per 1,000 children and youth with DSM IV diagnoses rated as "severe." Although Massachusetts fares better than other States with 21.3 child psychiatrists per 100,000 children and youth (national average is 8.6), in the past satisfaction has been low. In one study 33 percent of families waited one year or more before receiving mental health treatment. Two-thirds of primary care providers (PCPs) reported appointment delays for mental health referrals averaging three to four months, with many complaints of dissatisfaction with professional communications from child psychiatrists.

The Massachusetts Child Psychiatry Access Project (MCPAP) is a system of regional children's mental health consultation teams designed to help primary care providers meet the needs of children with psychiatric problems.

In 2003 the Center for Medicare & Medicaid Services (CMS) and MassHealth funded a pilot program by Dr. Ron Steingard to provide consultations in central Massachusetts around child psychiatry problems. In 2004, the Massachusetts Behavioral Health Partnership (MBHP), the MassHealth behavioral health vendor, and a service center of ValueOptions adapted the program for a statewide rollout with a budget of approximately $3 million. The project received legislative support with assistance from advocates, providers, insurers, State administrators and academic centers. The project was funded through the Department of Mental Health.

Design

Six regional teams with 1.0 full-time employee (FTE) child psychiatrist, 1.5 FTE social worker/psychologist, and 1.0 FTE care coordinator were needed for implementation. All 1.5 million Massachusetts children, without regard to insurance, are eligible for MCPAP services. Telephone consultation is provided Monday-Friday, 9:00 a.m. to 5:00 p.m. within 30 minutes of a request. Each PCP signs an agreement to cooperate with the MCPAP educational program and to provide prescribing for appropriate cases. The team provides ongoing education to PCPs based on their need. MBHP provides electronic medical record and data collection, and evaluates the program based on encounters and PCP satisfaction. Numerous other services including organized continuing medical education (CME) and a Web site (www.mcpap.org) are provided.

Program Cost

The program began with six teams, 331 practices, and 1,237 FTEs of primary care providers. More than 14,000 encounters in fiscal year (FY) 08 and more than 96 percent of the children in the Commonwealth were covered. Only two percent of PCPs refuse to participate. The total costs were $3 million per year or $0.17 per child per month.

Measured Results

Phone consultation with PCP–46 percent; care coordination–21 percent; face-to-face evaluation–16 percent; phone to member/family–10 percent; follow-up visit–6 percent; other–1 percent.

Outcomes

PCP satisfaction measured by surveys before and after the program showed marked increase in satisfaction across many domains. There was strong provider support for the program as measured by surveys.

Lessons Learned

- Providing consultation and education about child psychiatry to PCPs will relieve problems with access to child psychiatry
- Well-designed co-location works best
- Not payer-based works best
- Use academic, not community psychiatrists
- No prescription pads, consultation only
- Need an administrator who is accountable statewide

Mature Practice

Criterion:	Mature practice
Evidence:	Peer-reviewed study[1]
Maturity:	began in 2002
Dissemination:	Active throughout MA by design; being applied (modified) in WA and IL
Cost	Saving not measured; marked increase in quality
Access:	Marked increase
Acceptance:	By providers high; by members unmeasured
Implementation:	Requires significant planning and coordination
Outcomes:	Documented by increase in PCP satisfaction across many domains

For More Information

E-mail MaryEllen Foti at maryellen.foti@dmh.State.ma.us.

[1] Connor DF, McLaughlin TJ, Jeffers-Terry M. Targeted child psychiatric services: A new model of pediatric primary clinician–child psychiatry collaborative care. *Clin Pediatr* 2006:45:423-434.

Missouri: Benchmark Reporting in BPM Intervention Mature Practice

Background

The Missouri implementation of CNS' BPM program includes a series of custom-designed benchmark reports comparing individual prescribers as well as group practices.

Design

Physicians who prescribe a significant volume of behavioral health medications receive an individual Benchmark Report with their monthly BPM Quality Letter, which contains additional information on their percentage of outlier prescriptions, a numerical and percentile rank comparison to other high volume providers, and a list of the number of the provider's patients and prescriptions that were involved in each Quality Indicator during the designated reporting period. Each Quality Indicator identifies a particular prescribing practice that is considered to be outside of best practices guidelines. In addition to these individual reports, a Group Practice Benchmark Report is provided monthly to the directors of Missouri's Community Mental Health Centers and quarterly to the directors of Missouri's Habilitation Centers, which promotes improvement of behavioral health prescribing practices for complex need patients in these settings. The report lists the percentage of outlier prescriptions written for each agency's patients during the designated reporting period.

Finally, for State-level administrators, a Prescriber Detail Report provides extensive information on the nature of all outlier Medicaid prescriptions by prescriber. For each physician with outlier prescriptions, the report provides the total number of patients served by that physician and the total number and cost of claims, plus, for scripts that triggered a Quality Indicator, a description of the specific QI, the count of the prescribers patients associated with those scripts, and the associated costs of those claims.

Development Timeline

Each took approximately one year initially and has been revised and improved subsequently.

Program Cost

The reports are part of the overall BPM program.

Measured Results

The benchmark metric, the number of psychotropic prescriptions involved in a potentially questionable practice, calculates percentile rankings divided by all psychotropic prescriptions reported for both raw counts and percentile rankings.

Outcomes

Initial report revealed a threefold variation across Community Mental Health Centers (CMHCs) (6 percent to 18 percent outliers). In the first year after implementation, there was a 3 percent overall reduction in the percentage of outlier prescriptions by CMHCs.

Lessons Learned

Following group discussions, it was agreed that the agencies would all be individually identified in the outlier reports, thus allowing everyone to see where everyone else stood in the rankings. CMHC managers reported that this was a very helpful tool to engage their psychiatric staff discussions of practice quality of the information. It was also useful for meeting certification requirements for drug utilization review (DUR). Individual psychiatrists have also been accepting and appreciative of the benchmark information.

Mature Practice

The use of benchmarking in quality improvement, in general, has a long history and a robust published literature proving its efficacy. The use of benchmarking specifically applied to prescribing practices in Missouri has more than one implementation, has been going on more than three years, has documented improvement in quality and cost savings, has good provider acceptance, and is proven straightforward to implement.

For More Information

Visit http://www.dmh.mo.gov/MHMPP/MHMPP.htm or e-mail Joe Parks at Joe.Parks@dmh.mo.gov.

Oklahoma: SoonerPSYCH Behavioral Health Rx Management Promising Practice

Background

SoonerPSYCH (Prescription Solutions for Your Cognitive Health) is the Oklahoma version of the BPM program performed by Comprehensive NeuroSciences, Inc. (CNS). Oklahoma started this program in 2004 to provide education and claims information to prescribers of behavioral health medications. SoonerPSYCH is co-sponsored by the Medicaid and mental health agencies in Oklahoma—Oklahoma Health Care Authority (OHCA) and Oklahoma Department of Mental Health and Substance Abuse Services (ODMHSAS).

Development Timeline

- Oklahoma Medicaid, known as SoonerCare, experienced a major change in January 2004, as members who had previously been assigned to managed care plans were transitioned into a single fee-for-service pharmacy program. OHCA and CNS started working out data exchange details early that year and the first mailings to providers were done in August.
- Prior to the start of the mailings from CMT, the medical director for ODMHSAS created a three-hour CME-accredited program. She took the program around the State to mental health practitioners on the Red Dirt Road Tour, explaining the concepts of evidence-based treatments, best practices, and expert consensus guidelines. Most of these presentations took place at CMHSs, but other providers in the area were also invited to attend.
- Mailings for the first year were focused on adult members only. Beginning in March 2006, mailings to children's prescribers were implemented every other month, alternating with mailings to adult prescribers. For the period of March 2007 to March 2008, mailings were focused only on the children's prescribers. In October 2008, the program was restructured from the BPM-type intervention to the Medical Risk Management program.

Program Cost

Total payments to CMT for this four-year program are just over $2 million. The bulk of the cost was for the first year, when data matching and technical resources were required. Eli Lilly, Inc. funded SoonerPSYCH. A direct payment was made to CMT by Lilly. No State funds were used directly for this program. However, the data matching and extracting process does require a significant amount of State staff time, as does answering questions and concerns from providers.

Measured Results

The program was tracked and measured using standardized reports from CMT. In addition to tracking the number of members utilizing certain medication classes, there are over 20 Quality Indicators that are measured and tracked. Reports are generated for a rolling three-month period, each ending with the most recent month of data. The table below shows a comparison between the quarter ending December 2004 and the quarter ending December 2007. The "Percent Pop" columns indicate the percentage of children utilizing at least one medication from the listed class

from the total child population for the last month of the quarter. The final column shows the change from 2004 to 2007.

Several data elements from the data dictionary could be used to measure the effects of this program: Prescribed AP, AP at ≤ 5 years of age, High Dose AP, Multiple APs.

Drug Class	Dec. 04	Percent Pop	Dec. 07	Percent Pop	Change
Any Atypical Antipsychotics	5,901	1.65%	7,148	1.77%	0.12%
Any Typical Antipsychotics	74	0.02%	63	0.02%	-0.01%
Any Anxiolytics/Sedative Hypnotics	2,032	0.57%	3,012	0.75%	0.18%
Any Antidepressants	7,880	2.21%	7,238	1.80%	-0.41%
Any Anticonvulsants/Mood Stabilizers	3,613	1.01%	3,331	0.83%	-0.18%
Any Sympathomimetics/Stimulants	13,848	3.88%	14,967	3.72%	-0.16%
Any ADHD Non-Stimulant	3,236	0.91%	2,101	0.52%	-0.38%

Lessons Learned

The most significant lesson we learned was the importance of the agency partnership approach, coupled with the exceptional educational component from ODMHSAS. Without their participation and support of the program through their educational efforts, we believe the program would have had serious opposition from the provider and advocacy community. Because we implemented only after meeting with a large number of stakeholders, where program goals were clearly communicated to providers and advocate, we believe the program was well accepted and successful in improving the quality of care for our members.

Promising Practice

The SoonerPSYCH, or BPM-type program, is a promising practice because of the evidence, maturity, dissemination, acceptance, and implementation criteria:

- Evidence: at least one implementation site with data showing desirable results
- Maturity: the program was in place for about four years
- Dissemination: the program was implemented in several States and data is available from at least three States (Oklahoma, Utah, and Missouri)
- Acceptance: members were not directly affected, so their acceptance could not be measured. However, since their access to medications was not affected, we believe they would generally be accepting of the program in that their care would be improved. Providers were generally accepting of the program; however, if they requested that they be removed from the mailing list, that request was honored.
- Implementation: fairly straightforward, some data kinks to work out, but otherwise simple. Did not require policy changes, legislative action, or funding review.

For More Information

E-mail Paul Keenan at Paul.Keenan@okhca.org.

Oklahoma: SoonerCare Medical Risk Management Emerging Practice

Background

The ODMHSAS and the OHCA implemented a program called Medical Risk Management (MRM) for SoonerCare members under the age of 18 who have been diagnosed with schizophrenia and a co-occurring medical disorder.

MRM is patient focused and designed to keep physicians and case managers informed of medical and psychiatric issues arising in each patient's care. Care Management Technologies (CMT) is the vendor who performs the data analysis and mailings for the program.

MRM utilizes predictive risk modeling for pinpointing which patients with schizophrenia are trending toward high-risk/high cost disease States, allowing existing provider systems to proactively focus appropriate clinical interventions. CMT utilizes medical, behavioral services, and pharmacy claims data to identify targeted patients most in need of intervention.

MRM provides *Integrated Health Profiles* on a regular basis to keep physicians and case managers alerted to patient care issues such as:

- Emerging patient health risks
- Potentially dangerous drug-drug interactions or side effects
- A comprehensive list of the patient's prescriptions
- Recent medical and psychiatric outpatient visits
- Recent emergency room and hospital admissions

After patients are identified, the MRM program will determine if they have a "psychiatric home" such as an CMHC program already serving them. If not, they will be referred to the appropriate CMHC in their area. In addition, MRM will determine if each patient has a "medical home" such as a physician who is serving as the patient's primary medical care coordinator. If not, an MRM health liaison will assist in finding a primary care provider.

Development Timeline

- In October 2008, CMT began mailing packets on approximately 600 children.
- There was a short period of time required to determine if there were SoonerCare members selected for the MRM project who were already involved in one of the other care coordination projects at OHCA. Members were excluded from the MRM program if they were included in another program.

Program Cost

- Payments to CMT for this program have been less than $500,000 per year.
- The MRM program was funded by Eli Lilly, Inc. A direct payment was made to CMT by Lilly. No State funds were used directly for this program. However, the data matching and extracting process does require State staff time.

Measured Results

The analysis for this program is pending. The expected outcomes of the MRM program include:

- Greater patient adherence to medication plans (physical and behavioral)
- Fewer unplanned urgent, emergent and inpatient hospitalization events
- Lower overall health care costs per patient when compared to costs of comparable patients not involved in the MRM program
- Healthier patient with a better quality of life

Lessons Learned

Many children enrolled in the SoonerCare program experience fractured systems of care. This project attempts to get all providers on the same page with respect to mental and physical health conditions and treatments.

Emerging Practice

The MRM program is an Emerging practice because:

- Evidence: at least one implementation site with data showing desirable results
- Maturity: the program has been in place for about 1.5 years
- Dissemination: the program has been implemented in at least two States. Data available has not been formally analyzed at this point.
- Acceptance: members are not directly affected, so their acceptance cannot be measured. Providers have been generally accepting of the program
- Implementation: fairly simple and straightforward, most data problems had been settled with previous programs. Did not require policy changes, legislative action, or funding review.

For More Information:

E-mail Paul Keenan at Paul.Keenan@okhca.org.

Washington: Provider Access Lines (Phone-Based Consultation) Promising Practice

Background

PCPs often provide primary mental health services to children, in large part because they have limited access to child mental health specialists. Creating a collaborative care arrangement among PCPs and a limited number of child mental health specialists may be an effective way to support, educate, and enhance the ability of PCPs to provide basic mental health services, even when there are few local resources available.

Washington State created a collaborative care program to address this very need called the Partnership Access Line (PAL). The design of Washington State's collaborative care and access program models the Massachusetts Provider Education Program (MCPAP). The pilot is similar to the MCPAP in scope; however, it differs in that WA Medicaid uses a single center for calls through the Seattle Children's Medical Center Department of Psychiatry rather than several local resources. At this time the pilot is available in two regions. These regions were chosen due to higher than expected utilization of mental health medication (high dose and poly-pharmacy). The program is marketed with an emphasis on foster care; however, there are no restrictions related to insurance status. The nature of the conversation between PCP and PAL consultants is best characterized as a "curbside consult" in style, but in substance it offers much more than a simple curbside. PAL consultants are expected to hold their advice to an evidence-based standard, using regular consultation group meetings to review currently available evidence based assessment and treatment information and to assure consistency across consultants. Consultant recommendations are based on a child mental health care guide developed specifically for this program and distributed to PCPs. One early measure of feasibility is overall utilization of the program. The program is featured on www.palforkids.org which contains contact information as well as a resources section with State agreed clinical algorithms.

Development Timeline

It took nine months to contract and build infrastructure for the lines. During the building, provider education and marketing began based on the mental health treatment and new mental health guidelines that were a strong marketing source.

Program Cost

The funds stem from a bill (SB1088) to improve mental health access. The PAL line had a budget line of $1.3 million.

Measured Results

Under PAL there are provisions for customer services (waiting and call back times) as well as reports on referrals, client types, issues and outcomes. A provider satisfaction questionnaire recently showed strong support. The program is tracking prescription changes, referrals for consultations, and inpatient evaluation recommendations. Thus far one in 10 consultations have led to a face-to-face review and exam. So far the PAL reviewers think that evidence based

treatment through consultations is giving raise to less expensive care that usual care. Each consultation begins by the PCP calling a toll free number that is answered by one of two assistants who work with the program. Over the first seven months of the program PAL has performed well over 300 phone consults originating from more than 150 providers. Of the calls received 17 percent were for kids 0-6 years old, 39 percent for kids 6-12, and 44 percent were for kids 12-18 years old. We have also provided local CME mental health education to over 170 providers (many of whom subsequently called our program). We have also begun to collect survey data relevant to feasibility and satisfaction. We have received 26 satisfaction surveys as of October 2008. These pilot data are quite positive with an overall average satisfaction/feasibility rating of 4.82 (SD = 0.32) on a 5-point scale (5 indicating the highest level of satisfaction/feasibility).

Qualitatively primary care providers using the program have been quite vocal in their support of the arrangement, saying things like, "It has been so incredibly awesome to have you guys," and "The service is very valuable to me. I'm so glad I can call!" Qualitatively, the consultations questions thus far cover a wide range of topics and over half the time the primary consultation question is medication requests.

Outcomes

In the first seven months the PAL had 300 calls from 150 providers treating children (58 are in foster care).

Lessons Learned

Timelines for building this project are slow for the following reasons: (1) child and adolescent psychiatry resources are scarce and therefore competes for time with clinical duties, (2) marketing is more by word of mouth and typical mail FYI has been ineffective in boosting consolations, (3) mental health and psychiatry need to be at the table for design and implementation to ensure integration, (4) funding should be built in the Medicaid claims budget rather than an admin budget to ensure it is resistant to budget cuts, and (5) PCPs are more comfortable with telephone-only advice from PAL than we expected. To our knowledge, Washington is the first State to replicate and adapt the Massachusetts MCPAP child mental health consult program. Washington's PAL provides rapid child mental health consultation and resource connection assistance to primary care providers over a very large geographic area with few specialist resources, and has a unique emphasis on providing service assistance to the State's Medicaid population. There are plans for an extensive evaluation of this program for the University of Washington.

Promising Practice

This pilot program in two large rural Washington regions has improved access to children's psychiatric services. The program enjoys wide community acceptance as evidenced through provider and consumer surveys. The program costs and implementation are supported through a State statute and funding by the legislature. The consultations are integrated into the foster care and mental health clinic systems. Outcomes measures including Rx cost effectiveness are being tracked and appear to bring some cost effectiveness. Outcomes, including referrals to services,

juvenile justice, foster care stability and placements, sick days in school, medical and mental health costs, are being tracked.

For More Information

Visit www.palforkids.com or e-mail Jeff Thompson at ThompJ@dshs.wa.gov.

California: Use of the Web
Promising Practice

Background:

The California Mental Health Care Management Program (CalMEND) was established in 2005 as a quality improvement program to promote wellness and recovery for individuals with mental illness. Supported by funds from California's Mental Health Service Act (MHSA), CalMEND operates under the sponsorship of the California Department of Health Care Services (DHCS) Pharmacy Benefits Division, in collaboration with the California Department of Mental Health. In 2007, CalMEND established a Web site www.calmend.org dedicated to the communication and dissemination of CalMEND news, program development and initiatives, including best practices and transformative changes.

Development Timeline

Three months.

Program Cost

$5,000 start up cost which included expenses associated with purchasing of hardware and software needed to launch the www.calmend.org Web site. Ongoing maintenance is budgeted at about four hours per week of staff time.

Funding Source

MHSA funded the cost of Web site designs, implementation and maintenance. DHCS and the Department of Mental Health provided the staff to support content development.

Performance Metrics

Quarterly reports on site visits and other statistics are collected to monitor the usage of this Web site.

Trends Changed

Traffic to the Web site (number of hits) has increased over time. The length of time spent on the Web site (depth of activity) has also increased. The number of inquiries (phone and emails) has also increased over time.

Lessons Learned

- Use of the Web is an efficient and cost effective way to inform the public on the development of CalMEND.
- Having a distinctive Web address— www.CalMEND.org—increases ease of access to the CalMEND program.

For More Information

Visit www.CalMEND.org.or e-mail Penny Knapp at Penny.Knapp@dmh.ca.gov.

Colorado: Use of the Web Unclassified Practice

Background

Colorado Medicaid posted information about a two-year project conducted with Comprehensive NeuroScience (CNS) and is available on its Web site at http://www.colorado.gov/cs/Satellite/HCPF/HCPF/1201542571182. The project ran from July 1, 2006 through June 1, 2008.

In order to offer assistance in the establishment of quality-based mental healthcare, Colorado Medicaid has posted a link to the Florida Best Practices Medication Guidelines on its Web site at (http://flmedicaidbh.fmhi.usf.edu/recommended_guidelines.htm). The link allows providers the ability to easily access the guidance provided by these suggested practices. In addition, CNS used these guidelines in establishing their quality indicators and Colorado Medicaid posted them on their Web site for providers interested in more background about the CNS program.

Development Timeline

The development of a timeline was not applicable to the posting of the links or information on the Web site for Colorado Medicaid.

Program Cost

There was no cost to post the links or information on the Web site for Colorado Medicaid.

Measured Results

No data were collected and no measurements of performance were conducted regarding the Web site postings.

Outcomes

No outcomes were scientifically measured regarding the Web site postings. Colorado Medicaid received informal feedback that providers appreciated having the information available on the Web site.

Lessons Learned

The Department is looking into expanding the information on the Web site. The Department plans to discuss what would be useful with interested stakeholders.

Unclassified Practice

Offering clinical resources on the department's Web site is new to the community. It is unknown if the service will provide cost effectiveness, improve quality, improve access, or show improved outcome measures but Colorado is optimistic that providing and expanding the clinical

resources available to our providers will be of benefit. There are no barriers to implementation. The clinical community has expressed appreciation for the service.

For More Information

E-mail Kimberly Eggert at kimberly.eggert@State.co.us.

Maine: Edits at Point of Sale Leading to Mandatory Filing for Prior Approval
Promising Practice

Background

Maine's PDL was implemented in July 2003. A PDL, unlike a formulary, has all drugs included in it with non-preferred drugs available under specific circumstances, through a prior approval (PA) mechanism. For the most part, restrictions apply only to new starts with grandfathering of persons on established regimens. Edits are programmed into the system for obtaining Medicaid authorization at the point of sale, disallowing dispensing and requiring the filing of a request for PA. Requests for PA are then reviewed by a medical staff employed by the State's pharmacy management provider, with follow-up consultation to prescribers in specific cases. Preferred drugs must be tried and failed due to lack of efficacy or intolerable side effects before non-preferred drugs will be approved, unless an acceptable clinical exception is offered on the PA form, such as the presence of a condition that prevents usage of the preferred drug or a significant potential drug interaction between another drug and the preferred drug(s) exists.

Design

In Maine, especially in the early days of the PDL, designation as preferred or non-preferred was largely determined by a drug company's willingness to enter into cost-lowering contractual agreements with the State, so long as clinically equivalent non-preferred drugs were available. The list of preferred and non-preferred drugs that is driven by these cost saving negotiations generally changes once a year, after contract negotiations are complete. Quality and safety edits are added at various times during any year, after review of the evidence, deliberation by the DUR (and in the case of psych drugs, the Psychiatric Work Group), and publication of the new PA requirements in various mailings to prescribers. Quality edits regarding high and low dosage and within class and duplicate therapies were among the first quality edits implemented in 2006, but others continue to be added as evidence indicates. Thus the point of sale edit and PA process is a dynamic and evolving system.

With regard to psychotropic drugs, as of May 2010, quality edits limit concurrent prescribing beyond a 90-day cross-over period for two or more antipsychotics, selective serotonin reuptake inhibitors (SSRI's), benzopdiazepines and other within class drugs. In January 2007 a limited step therapy protocol for atypicals was implemented (and fully implemented by July 2007), requiring a trial of one preferred atypical before therapy with a non-preferred agent could be approved. At present, non-preferred atypicals that require a trial of one preferred agent include Risperidal Consta, Saphris, Fanapt and Invega. Preferred atypicals such as Clozapine, Seroquel or Zyprexa become non-preferred and require a PA if used in combination with Carbamazapine. Other quality edits include PA requirements for low dose Seroquel (to diminish utilization as a sedative hypnotic) and also for certain combinations of drugs where there is data on interference with metabolic degradation by liver enzymes when these drugs are prescribed in combination, (e.g., carbamazapine in conjunction with Ability, Clozapine, Seroquel or Zyprexa). In 2010, a PA requirement will be implemented for the prescription of any antipsychotic to a child under the age of 5, and in the planning stages is a requirement for PA for continued prescription of an

atypical antipsychotic beyond six months in the absence of any Medicaid service claim showing that glucose or lipid testing has occurred.

Potential quality edits are reviewed by the Psych Work Group, a DUR MaineCare supported advisory group comprised of consumer advocates and psychiatrists representing State mental health agencies, hospitals, community mental health centers, the Maine Medical Association, and NAMI Maine. The PA process is managed by GHS, the State's pharmacy management contractor. There are approximately 20,000 PA requests for all drugs in any given quarter. The wait time for review is, on average, 3.8 hours, with 75 percent of requests approved. Of 23,938 PA requests in the third quarter of 2007, 7.9 percent were for atypical antipsychotics and the remainders were for non-psychiatric drugs.

Development Timeline

The first edit for two or more drugs within a specific class for more than 90 days was started January 2006 and fully implemented by July 2006. The other quality edits have been ongoing.

Program Cost

Costs for programming the edits into the point of sale, medical review, and development of additional quality improvement initiatives are integrated into the contract between GHS and Medicaid. Support stems from the Psych Work Group and the DUR committee.

Measured Results

Data on utilization from the Child and Youth Antipsychotic study shows that overall utilization of antipsychotics did not change in the four years between 2004 and 2007 and that, overall, utilization of these drugs in Maine is in the top quartile compared to other States. Thus there does not appear to be a reduction in overall utilization of antipsychotics in the period in which the PDL and the PA processes were instituted. While one study limited to the first year of implementation of the PDL suggested that there was an increase in gaps in therapy in Maine, longer-term four year tracking of gaps in treatment from the Child Antipsychotic study shows that Maine's rate of discontinuities is among the lowest of the 16 participating States, suggesting that adherence has not been adversely affected by the PA policy.[1] Thus, the institution of the PA process for antipsychotics does not appear to have negatively affected access or adherence. Maine's rates of antipsychotic poly-pharmacy and high dose antipsychotic prescribing is low compared to other States, suggesting that the PA requirements related to quality management have had the desired effect. Analysis of expenditures for antipsychotics has shown significant cost savings, even as overall utilization has remained stable.

Outcomes

Data has shown a decrease in rates of poly-pharmacy and high dose prescribing, with Maine rating amongst the lowest in the 16-State study. Gaps in adherence have remained stable and low. Introducing quality edits has therefore had the intended effect of improving quality and safety without sacrificing access or continuity. What is lacking is data on psychiatric outcomes, e.g., on impact of changes in policy on psychiatric emergency room use or hospitalization, or family or school function. Additionally, there was an increase in the number of children

diagnosed with diabetes, raising concerns about atypical antipsychotics and long term health issues, which have been highlighted as a potential factor in the 25 year premature mortality of adults with Serious Mental Illness. Maine hopes to join with other States in the next stage of analysis of antipsychotic use across the lifespan, with inclusion of data on both psychiatric and health outcomes.

Promising Practice

The use of the PA process to guide quality and safety has been in place statewide for the past four years. Data from the Child Antipsychotic Study has shown improvements in quality of prescribing without change in access or discontinuities. Although members and providers were skeptical in the early stages of implementation of the PDL, the utilization of the PA process has gained more widespread acceptance, as a result of greater collaboration with the mental health community, broader educational programs, greater knowledge about the dangerous side effects of the atypicals, and efforts to reduce the administrative burden on psychiatrists treating the sickest populations.

For More Information

Visit www.mainecarepdl.org and www.ghsinc.com or e-mail Elise Freeman at Elsie.Freeman@maine.gov.

[1] Soumerai SB, Zhang F, Ross-Degnan D, et al. Use of atypical antipsychotic drugs for schizophrenia in Maine Medicaid following a policy change. *Health Affairs* May/June 2008:27(3):w185-w195.

Missouri: Prior Authorization (PA) of ADHD Medications Unclassified Practice

Background

Missouri's prior authorization of ADHD medication is a clinical edit process focused primarily on ensuring appropriate utilization utilizing clinical criteria.

Design

The edit process uses pharmacy claims data analysis of the prior three years as well as physician and hospital claims allowing that most requests be adjudicated without requiring prescribers to send additional information. The approval criteria are age banded with separate criteria for under 6 years old, 6 to 18 years old, 18 to 23 years of age, and over 23 years of age. Approval under 6 years of age requires use of standardized rating scale. Approval of an ADHD medication over 23 years of age requires psychiatric consultation for initial diagnosis and treatment initiation and may require use of the standardized rating scale. Persons with prior claims for substance abuse disorders, use of benzodiazepines or three or more psychiatric medications are flagged for clinical consultant review.

Development Timeline

The ADHD clinical edit took approximately 18 months to develop. Feedback was obtained at several points in the process from DUR and PA public committee hearings. An expert work group was formed to review literature and develop the criteria.

Program Cost

Unknown.

Measured Results

Unknown.

Lessons Learned

Program still in development.

Unclassified Practice

Program is still in development and no results have been achieved.

For More Information

E-mail Joe Parks at Joe.Parks@dmh.mo.gov

New Hampshire: E-Prescribing Emerging Practice

Background

New Hampshire's e-prescribing program began as part of its pharmacy benefit management services. In order to realize the benefits of e-prescribing, the prescriber must have access to a patient's drug history and alerts regarding potential adverse drug events. Eventually, individual payer management tools will be available through e-prescribing (e.g., prior authorizations, quantity limits, etc.). When available, these tools will further reduce adverse events and markedly reduce prescriber and pharmacist administrative burden. The NH Medicaid program and its pharmacy benefit administrator, First Health Services, Inc, jointly managed the project.

Development Timeline

It took six months to initiate the intervention.

Program Cost

The initial cost of creating the database to hold formulary and clinical information was approximately $64,000 and $0.14/drug transaction. Funding came from existing PBA administrative funds. No new funding was used.

Measured Results

The performance metrics include the number of prescribers currently accessing the database, monitored quarterly.

Outcomes

The number of prescribers fully capable to e-prescribe in NH is still small. It's anticipated that with the Medicare requirement to e-prescribe, the number of prescribers will increase. Additional outcomes could be better adherence to the Medicaid program's preferred drug list; however, many more prescribers would be needed. Generic utilization is already quite high in the State of NH; it is not expected to significantly increase due to e-prescribing. The Medicaid program does not monitor adverse drugs reactions.

Lessons Learned

The project was remarkably cheap and easily implemented. NH Medicaid has enabled prescribers to use e-prescribing for beneficiaries. The next steps belong to prescribers.

Emerging Practice

The number of prescribers is still small and the impact on prescribing patterns has not been measured.

For More Information

E-mail Doris Lotz at dlotz@dhhs.State.nh.us

New York: PSYCKES, Prior Authorization, and Feedback Promising Practice

Background

The New York State Office of Mental Health (OMH) developed and implemented a phased approach to improving prescribing practices in its entire network of 26 State-operated inpatient psychiatric hospitals.

- Phase I: PSYCKES Implementation—The Psychiatric Services and Clinical Knowledge Enhancement System (PSYCKES) was developed and implemented in all OMH-operated State hospitals. PSYCKES provides access to client-level data derived from State administrative pharmacy databases, summarizing individual treatment histories back to 1989 and flagging questionable practices. PSYCKES also measures performance on guideline-derived quality indicators at the State, hospital, ward, and prescriber levels.
- Phase II: Prior Authorization—After PSYCKES was implemented, PA was established by the Office of the Medical Director in April 2005. This policy required written PA by the OMH Medical Director for use of three or more antipsychotics; it did not, however, block prescriptions from being filled.
- Phase III: Feedback—Six months after instituting PA, feedback to hospital clinical and administrative leadership was established. On a quarterly basis each hospital executive director and clinical director received a list of patients on three or more antipsychotics. Performance on this measure was discussed in quarterly meetings among hospital leadership and OMH central office leadership.

Development Timeline

PSYCKES was developed by an in-house OMH team for State-operated inpatient units in 2002-2003. First, quality measures were established and then end users engaged with prototyping reports, focus groups, and other readiness activities. The programming for the Web-based version of PSYCKES occurred in 2003, and was implemented in 2004-2005. As above, PA was established in April 2005 and six months later feedback to hospital leadership was initiated.

Program Cost

- Costs were attributed to dedicated personnel supporting the project:
- Senior Project Director–.5 FTE x four years
- Senior programmer–one FTE x one year for development
- SAS programmer/data analyst–one FTE x one year; 0.5 FTE x one year for evaluation; 0.25 FTE ongoing for maintenance;
- Field worker/ technical assistance–one FTE x two years; 0.1 ongoing

Measured Results

- To evaluate the impact and success of the project we used the following measures:
- Participation rates at the hospital and prescriber level—tracked via requests for access
- Rates of use—tracked via usage logs

- Impact on prescribing practices, specifically use of antipsychotic poly-pharmacy—tracked via PSYCKES

Outcomes

- Participation rates:
  - 100 percent of hospitals that offered access to PSYCKES requested access.
  - Prescribers were a target end user group and 75 percent requested access.
  - Rates of use of PSYCKES: use remained stable after implementation over a two-year period of study, with 30 percent of enrolled users logging on each month.
  - Clinical supervisors had the highest level of use.
- Impact on prescribing practices:
  - Overall prevalence rates of antipsychotic poly-pharmacy of three or more decreased 85.1 percent
  - Awards helped to document acceptability and impact of the project.
  - Governor's Workforce Champion Award for improving the work life of staff (prescribers)
  - Council of State Governments Award for Innovation
  - Based on the success of the project, OMH was funded for an expansion to the State Medicaid system statewide, focusing on poly-pharmacy in youth and adults

Lessons Learned

- Stakeholders, including prescribers, are interested in having access to administrative data for the purposes of managing clinical care and improving quality.
- PSYCKES can be used as a tool to improve quality and efficiency.
- Mandates alone may move practice, but not as significantly as when these policies incorporate monitoring and feedback.
- Evaluation of clinical impact and economic modeling can help to secure ongoing and enhanced funding for quality improvement.

Promising Practice

Data are available to support impact, have been presented at professional conferences, and are currently being prepared for publication. The project is mature (fully implemented by October 2005), and has been expanded to 337 outpatient mental health clinics. Impact can be assessed for all sites through PSYCKES. The project yielded both cost savings and quality improvement. PSYCKES have high levels of acceptance as evidenced by State and national awards, high participation rates, usability ratings, and stable usage rates over a two year follow-up period. PSYCKES was initially developed and implemented by an in-house team without additional resources, however, may require additional resources depending upon State. Some States have barriers to data sharing beyond the Health Insurance Portability and Accountability Act (HIPAA) that create challenges to implementation.

For More Information

E-mail Molly Finnerty at COMDMTF@omh.State.ny.us.

Pennsylvania: Prior Authorization of Olanzapine
Mature Practice

Background

In August of 2005, the Pennsylvania Office of Medical Assistance Program's Fee-For-Service Pharmacy and Therapeutics Committee (P&T) reviewed the atypical antipsychotics as part of the PDL process. Whenever behavioral health drugs are reviewed, the P&T Committee adds several psychiatrists as voting members. The Committee includes a physical health and behavioral health consumer as voting members. The consumers also have a voting physician advisor.

At the Committee meeting there was general discussion about the efficacy of the newer antipsychotics and their side effects, especially since the CATIE study was about to be released. This study indicated that olanzapine was associated with greater weight gain and metabolic side effects than other antipsychotics. There was concern about utilization of this drug in adults and especially in Pennsylvania's Medicaid pediatric population that already exhibited a 15 percent rate of obesity and a 17 percent rate of being overweight. The P&T Committee recommended olanzapine undergo prior authorization requiring the trial and failure of one preferred antipsychotic by adults and children before trying olanzapine. Existing recipients were grandfathered and allowed to continue their medication without prior authorization.

Development Timeline

The Committee made its recommendation in August of 2005. The recommendation was presented publicly at the Pennsylvania Medical Assistance Advisory Committee and then underwent a public comment period. After reviewing public comment, the Secretary of the Department of Public Welfare, Estelle Richman, approved the recommendation. A Medical Assistance Bulletin describing the list of preferred and non-preferred drugs as well as the prior authorization process was published in November of 2005 (see Web links below). From August to November, system changes were made to the MMIS claim payment system so that pharmacies would know via hard edit at the point of sale that prior authorization of olanzapine was required for non-grandfathered recipients. The program was implemented in November of 2005. See the following Web sites for details:
http://www.dpw.State.pa.us/PubsFormsReports/NewslettersBulletins/003673169.aspx?BulletinDetailId=1071
http://www.dpw.State.pa.us/PubsFormsReports/NewslettersBulletins/003673169.aspx?AttachmentId=4418

Program Cost

Implementation costs were minimal (<$10,000) since no new staff positions were added to the existing pharmacy management unit in the Bureau of FFS Programs. Costs were associated with MMIS system changes, notices to providers and internal training.

Measured Results

The following pediatric metrics were developed to assess the program—unique recipients receiving the drug by age, percent of recipients receiving olanzapine that are on any antipsychotic (market share), total cost for olanzapine per year, and average cost of olanzapine per recipient.

Outcomes

Unique recipients receiving olanzapine were reduced from 2004 to 2007

	2004	2005	2006	2007	Percentage of Reduction
Age <5 Years	50	27	18	8	**-84%**
Age 6- 11 Years	535	355	186	124	**-77%**
Age 12 - 18 Years	1,215	763	503	384	**-68%**
Total	**1,800**	**1,145**	**707**	**516**	**-71%**

Market share of olanzapine was significantly reduced. Market share was defined as the number of recipients receiving olanzapine divided by the number of recipients on any antipsychotic

	2004	2005	2006	2007
Total on olanzapine	1,800	1,145	707	516
Total on antipsychotic	9,473	10,442	11,168	12,032
Percentage on olanzapine	19.0%	11.0%	6.3%	4.3%

The total cost for olanzapine per year and average cost of olanzapine per recipient were both significantly reduced

Year	Unique Recipients	Paid Amount	Avg. Paid Per Recipient
2004	1,800	$2,455,407.09	$1,413.59
2005	1,145	$1,701,119.64	$1,545.07
2006	707	$983,008.56	$1,535.95
2007	516	$708,541.02	$1,373.14

Lessons Learned

Engaging the psychiatric community, consumers, and other stakeholders in the discussion of prior authorizing olanzapine was essential to successful implementation of this initiative. To assure an adequate safety net, availability of a five-day emergency supply and grandfathering of current consumers was allowed.

Implementing prior authorization of olanzapine based on clinical quality concerns about metabolic syndrome and childhood obesity resulted in: reductions of unique olanzapine users, reduced market share, and reduced spend on this drug. Unfortunately overall utilization of antipsychotics in children has continued to increase in Pennsylvania and market share has shifted significantly to another branded product (aripiprazole).

Mature Practice

The initiative was implemented in a relatively short time frame, has proven to be effective over the past 3 years in reducing utilization and cost of a drug with concerning side effects, and has generally been accepted by the provider community and consumers.

For More Information

E-mail David Kelley at c-dakelley@State.pa.us.

Washington: Second Opinions
Mature Practice

Background

The appropriate use of psychotropic medications in youth is an important public health concern. We built a review process in Washington State to monitor the use of attention deficit hyperactivity disorder (ADHD) drugs in youth receiving fee-for-service Medicaid services. The program developed safety parameters for medications based on a process involving clinicians, community providers, consumer advocates, and industry. A second opinion by a community psychiatrist was mandated for all prescriptions above safety thresholds (e.g., dose, combination therapies, or < age 5). Utilization and cost were compared two years before and after the program began. Pharmacy claims had edits to stop ADHD medication for new starts and initiate a second opinion for refills.

Development Timeline

The program was developed over approximately six months of discussion with the community. Implementation took approximately three months and included provider communication as well as provider training.

Program Cost

Funding for this program was accomplished through the Medicaid outpatient claims system. Second opinions were given a unique current procedural terminology (CPT) code at a rate of $225 per record review. Total costs of the program were approximately $100,000 with estimated savings of $1.1 million and a return on investment of 1:10. There was a strong Hawthorne effect in practice change.

Measured Results

Claims from the pharmacy system were used to monitor trends. A provider questionnaire was conducted to assess customer service and program outcomes showing good provider acceptance and customer service without an increase of fair hearings.

From May 2006 to April 2008, 5.35 percent of ADHD prescriptions exceeded safety thresholds, resulting in 1,032 second opinion reviews. Of those, 576 (56 percent) resulted in a prescription adjustment. Of the prescriptions adjusted, 322 (37 percent) were from primary care physicians, 86 (28 percent) were from psychiatrists, 54 (38 percent) were from nurse practitioners (ARNP), and 21 (38 percent) were from physician assistants. When the pre- and post-periods were compared, second opinions reduced ADHD medication utilization in children less than 5 years of age (23 percent), use of high dose (53 percent) and use of combinations (44 percent). The review process resulted in a savings of $1.2 million with 798 fewer patients exceeding safety thresholds. However, the overall Medicaid expenditures for ADHD medication still increased due to higher unit costs and the preferential use by clinicians of newer brands entering the

market. We are using these outcomes to put in place the AP second opinion process. The program will be measured in similar manner as ADHD medications (see table below).

Lessons Learned

A statewide second opinion process reduced outlier ADHD medication practices, was cost effective, and overall worked well with the community. Initially the program contracted with three children's regional hospitals. There were difficulties in maintaining good inter-rater reliability between these three centers. The program has been restructured and now contracts with a single hospital.

Mature Practice

This statewide second opinion is mature (>3 years), was built and well accepted by the clinical community as evidenced through a provider survey, was cost effective, improved quality, improved access to child psychiatry, was integrated into the claims system, thus making implementation and payments simple, and the outcome measures showed improvement (lower numbers of kids on too many, too much, or too young). The outcomes have been reviewed internally and were published in the the Journal of the American Academy of Child and Adolescent Psychology (JAACAP).[1]

The Pediatric Advisory Group agreed on the following thresholds based on a reveiw of the claims data reflecting the community prescribing practices. The following thresholds have been incorporated into the clinical guidelines:

- Absence of an of DSM-IV diagnosis in the child's claim record
- Children less than 5 years of age receiving antipsychotic and ADHD drugs
- Five or more psychotropic medications prescribed concomitantly after 60 days
- Two or more concomitant antipsychotic or ADHD medications after 60 days
- Three or more concomitant mood stabilizer medications
- Prescribed psychotropic medication is not consistent with appropriate care
- Psychotropic poly-pharmacy for a given mental disorder is prescribed before utilizing psychotropic monotherapy as new start noted from pharmacy claims data

Age and Dose Thresholds Requiring Second Opinions

Drug	FDA Max Dose				
		<3* Yrs	3-5* Yrs	6-12 Yrs	13-17 Yrs
Risperidone	16 mg	0	2	4	8
Olanzapine	20 mg	0	2.5	10	20
Quetiapine	800 mg	0	0	300	600
Ziprasidone	160 mg	0	0	80	160
Aripiprazole	30 mg	0	0	20	30
Clozapine	900 mg	0	0	600	900

Haloperidol		0	0	10	15
Perphenazine		0	0	12	24
Methylphenidate		Greater than 120 mg (any age)			
Dextroamphetamine		Greater than 60 mg (any age)			
Vyvanse		Greater than 70 mg (any age)			
Daytronna		Greater than 30 mg (any age)			
Strattera		Greater than 120 mg (any age)			
Combination use of SSRI and SNRIs		Restricted to failed mono-therapy and no dosing two SSRI or two SNRIs in combination			

*A zero would indicate the need for an expert opinion.

For More Information

E-mail Jeff Thompson at ThompJ@dshs.wa.gov.

[1] Thompson JN, Varley CK, McClellan J, et al. Second opinions improve ADHD prescribing in a Medicaid-insured community Population. *JAACAP,* July 2009;48:7:740.

Notes on Use of the Classification Matrix

The following matrix is designed to classify State activities through a series of categories that capture the scope and depth of the implementation. The intended use of the matrix is to determine where within the spectrum of achievement a current or contemplated State practice lies. The goal is to identify practices that have worked well or are believed likely to do so, and to highlight practices that are replicable in many States. The exercise is not intended to "rank" or "rate" a State's performance in response to the challenge of antipsychotic medication use in children.

"Mature" practices include those which have achieved acceptance because of their documented performance, but given the nature of innovation it is implicit that "promising" or "emerging" practices may in time prove more effective than those presently declared as "mature." In theory, a State presently engaged in a few established activities, for a variety of social, fiscal, or political reasons, may find that their activities are mature practices, while another State with more opportunities and resources, pursuing a number of aggressive and innovative measures, may find that their practices are promising or emerging. Neither condition is better or worse than the other. And for numerous reasons, an activity that has found great success in one venue may be impractical or unachievable in another.

Considerations in Using the Matrix

It is not expected that a practice will have all the properties listed within a single column. For example, a mature practice may have dissemination to only a few locations, possibly because of cost or difficulty in implementation, while another practice that has been taken up by many sites may have little information available about its efficacy and thus remain a promising practice. In each case, assignment will depend on the thoughtful judgment of the reviewer.

A single phrase or two describes most features of a practice. In two instances, "cost effectiveness" and "acceptance," it was felt that two contrasted qualities needed to be considered simultaneously. For example, initiatives to address matters of cost should not be assessed without recognizing the potential for impact on quality. Similarly, acceptance of a practice by providers may be divergent to acceptance by members (recipients). Both have a stake in the assessment of practices. We also considered the role of acceptance by implementers (i.e., State employees), but found that placement with concerns for the external stakeholders would be confounding. Concerns of Medicaid employees may be addressed in the "implementation" section.

There are undoubtedly other features of these practices that have not been addressed by this matrix. We felt the tension between completeness and usability of the tool. We hope that the features we have selected will be sufficient to achieve the goals of identifying useful activities of comparable quality, and that this endeavor will help in achieving optimum care for our youngest Medicaid members.

Table 1. Implementation Strategies Classification Matrix

	Mature Practice			Promising Practice			Emerging Practice	Unclassified
Evidence	Peer Reviewed. Published studies or detailed reports with methods and outcomes data showing clearly showing desired results. More than one study or report. Independent review(s).			At least one implementation site with data showing desirable results.			Implementation in at least one site. Data may be preliminary.	None
Maturity	Varies, but usually three or more years.			Varies. Usually within one-three years.			Less than one year to two years. Could be longer.	Usually less than year or could be in planning phase. Could be longer.
Dissemination	Multiple implementations (possibly of varying maturity). Geography depends on the practice.			One or more implementations, at least one site with data.			At least one implementation.	May still be conceptual.
Cost Effectiveness								
Cost	Net Saving		Wash	Net Saving		Wash	Uncertain	Unknown
Quality	Increase or same		Increase	Increase or same		Increase or same	Increase or same	Unknown
Access	Substantial shifts in access in the desired direction.			Shifts in access in the desired direction.			May show shifts in access in the desired direction; or does not shift untoward.	Unknown
Acceptance								
By Provider	Good	Fair	Good	Fair	Fair	Poor	Undetermined	Unknown
By Member	Good	Good	Fair	Good	Fair	Poor	Undetermined	Unknown
Implementation	Straightforward. Minimal review. Minimal additional costs. Most resources already in place.			May be straightforward, or may require agency or legislative review. May require budgetary increases and/or additional resources.			Significant perceived barriers of cost, acceptance, review and/or resources.	Unknown, but barriers expected.

Appendix I - Stakeholder Comments

HHSC solicited stakeholder input on a draft version of this report and received 20 responses, some generally supportive of the report and others critical of various aspects of the report. HHSC modified the final report based on the comments listed on this page, and the full text of all 20 responses is included as the remainder of this appendix.

Executive Summary, Section I – Conclusions and Options for Texas Medicaid, and Section V – Appropriateness, were modified based on the following comments:

- "This study does not address the paucity of psychosocial interventions for Medicaid recipients. Nor does it address that certain children are more likely to receive antipsychotics outside of treatment guidelines or fail to receive appropriate psychosocial interventions. Until these are addressed, children on Medicaid will continue to receive inappropriate, primarily medication-based treatment."
- "At some point, it might be desirable to include a statement about the lack of intensive behavioral interventions for the Medicaid population and how restrictions on inpatient length of stay may encourage increased antipsychotic use due to the need to stabilize a child quickly."
- "Major concern is that lack of parental compliance (e.g. not getting needed labs) may increase the risk to the child of taking these medications."
- "Ensure that the decrease in the use of antipsychotics related to the parameters did not have a negative impact on children by performing long term outcome studies."
- "Add that consultation could be done via telemedicine."
- "Provide training on the parameters to all current Medicaid child/adolescent providers."
- "The model to integrate mental health practitioners into pediatric clinics with a child psychiatrist as a back-up provide a model to help bring more psychosocial services to this population."
- "The summary (of pediatric comparison studies) should more strongly state that the number of subjects in these comparative studies was inadequate to conclude that there is no difference between the two generations of antipsychotics. Only a very large study can do this. As it reads now, the reader might think that FGAs are proven to be equally more effective."

Stakeholder Comments
H.B. 2163 Draft Report
Appropriateness and Safety of Antipsychotic Medications for Medicaid Children Under Age 16

(Commenters are listed in alphabetical order.)

Physicians Caring for Texans

Texas Pediatric Society
The Texas Chapter of the American Academy of Pediatrics

September 30, 2010

Lisa Kirsch Texas Health and Human Services Commission
P.O. Box 1324 Mail Code BH-4100 Austin, TX 78711

Dear Ms. Kirsh,

On behalf of the more than 44,000 physician and medical student members of the Texas Medical Association and the Texas Pediatric Society, we would like to thank you for the opportunity to review the draft report, *Safety and Appropriateness of Antipsychotic Medications for Medicaid Children Under Age 16*. We would first like to commend HHSC on the thorough review of the literature and your efforts in compiling this extremely comprehensive report. We would also like to lend our support to the comments submitted to you by the Texas Society of Child and Adolescent Psychiatrists, and emphasize a few areas of particular concern to our organizations.

As noted in the report, off-label prescribing is a well accepted medical practice and is no more common in psychiatric care than it is in general pediatrics. We would like to reiterate that it is essential for children to have access to medications prescribed in this manner, as their efficacy has been demonstrated though the drugs are not commonly tested in a pediatric population.

The report suggests that medications are not typically indicated until psychosocial interventions have failed. While this would be ideal, we feel it is important to acknowledge that there is a significant shortage of qualified child and adolescent psychiatrists, psychologists, and other mental health professionals to provide that type of therapeutic care. As such, medication may be an appropriate adjunct therapy in these situations. In addition to workforce shortages, Medicaid does not reimburse for services provided by Masters level therapists, who work closely with physicians to provide needed counseling and support services. Limiting reimbursement to PhD level therapists severely impacts access for Medicaid patients and, along with the shortage of qualified mental health providers, may contribute to an increased reliance

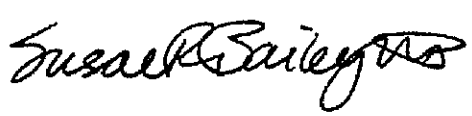
on medication.

We do not support the use of punitive measures such as prior authorization to restrict access to antipsychotic medications, and feel strongly that imposing administratively complex regulations may negatively impact both providers and patients of the Medicaid program. Increasing the administrative burden for prescribing medications will drive more physicians out of the Medicaid program, which will only exacerbate existing barriers to care for a population already dealing with significant unmet mental health needs. We fully support the recommendations to better educate physicians about the appropriate use of these drugs and to disseminate new clinical evidence as it becomes available; and our organizations are committed to working with HHSC on provider outreach efforts.

It is our goal to see that policy put into place will not serve to further exacerbate access to care issues or interfere with the decision making process of trained medical professionals – both of which we feel would be detrimental to patients. Please feel free to contact us with any questions, or let us know if our organizations can be of any service to you in the future.

We look forward to continued collaboration between HHSC and organized medicine to find ways to improve the availability and quality of mental health care for children in Medicaid.

Sincerely,



Susan Rudd Bailey, MD, President Texas Medical Association

Rick Lampe, MD, President Texas Pediatric Society

TEXAS MEDICAL ASSOCIATION 401 WEST 15TH ST AUSTIN, TEXAS 78701-1680 (512)370-1300 FAX (512)370-1630 **TEXAS PEDIATRIC SOCIETY, THE TEXAS CHAPTER OF THE AAP** 401 WEST 15TH ST, Ste 682 AUSTIN, TEXAS 78701-1665 (512)370-1506

Name: Joni Boyd, RN
Organization: West Texas Centers

Section/Page #/Line #(s) (as applicable)	Comment
Section I/pg 8 Line #13	Provide training on the Texas Parameters to all current
	Medicaid child/adolescent providers as some may be
	new to the Medicaid program since these guidelines were
	initially released in 2005.
Section I/pg 8 Line # 41	Consider the utilization of telemedicine to child/
	adolescent psychiatrists to facilitate these consultations
	for non-psychiatrist providers.
Section I/pg 9 Line #8,9	and to outline minimum training guidelines for all
	Medicaid practitioners.
Section I/pg 9 Line #16	HHSC will need to send out notification to all
	Medicaid providers regarding these new prior
	authorization requirements and the date that they
	will become effective.
Section I/pg8 Line #33	Ensure that all reviews are conducted by child
	psychiatrists and not by case workers or other
	non-medical personnel.
Section I/pg 8 Line #8	Ensure that the decrease in use of antipsychotic
	medication related to the wide distribution and
	application of the Texas Parameters did not have
	negative impact on these children by performing
	long term Outcome Studies.

From: John Breeding
Sent: Wednesday, September 15, 2010 8:23 AM

Thanks for sending this to me. I noticed a few of the findings on thh 2004-5 data that confirm the deep concern about this tragic drugging of our precious children with brain and body damaging antipsychotic drugs. I mention only two here.

1) The finding that over 37,000 children receive five or more psychotropic drugs concurrently is an absolute disgrace.

2) That so many of our very young chidren, younger than four or even three years old, are being given these drugs is so very sad and upsetting.

It is very clearly established that these drugs cause permanent neurological and metabolic damage in people who take them for very long, so the fact is that tthe state of Texas is badly hurting children in its care. The additional fact that these drugs do nor work in improving the lives and well-being makes it even more troubling. As Robert Whitaker lays out so clearly in his thorough reserach review book, *Anatiomy of An Epidemic*, what the drugs do is create permanent disability over time, and so that is what we are setting these children up for. This is why the orginial bill was to put a mild cautionary utilization check on the prescription of antipsychotic drugs to the children, and why we still need much greater protection and oversight. A law requiring a review of cases where children receive 3 or more of these potent drugs would be good. A ban would be the morally correct action.

Respectfully Yours,

John Breeding, PhD

Name: Regina Cavanaugh, MD
Organization: Texas Society of Child and Adolescent Psychiatry, President

Page	Comment
10	Off-label use is common in all specialties treating children and adolescents. Hopefully, industry and government will continue to support research and development, and FDA approvals for more medications will be coming
10	As guidelines for the monitoring of metabolic syndrome have been established for adults, there are recent guidelines pertaining to children and adolescents on antipsychotics.
11	Access to child and adolescent psychiatrists across the nation is a great concern. Having behavioral health specialists within pediatric/family practice offices, who are able to screen and help refer to psychiatrists, divert dangerous patients to inpatient units, assist in obtaining mental health services at all levels, utilize telemedicine in more rural areas, and facilitate consultation between psychiatrists and the primary care physicians would be helpful. I have been contacted recently by some our membership expressing the recent Medicaid psychiatric fee reductions have resulted in child and adolescent psychiatrists foregoing taking on new Medicaid patients, or choosing not to treat this population. Already members were complaining of the complexity of the patient population requiring more time for evaluation and medication management, lack of partial hospitalization services, even when inpatient was obtained there are no outpatient Medicaid providers to refer to after stabilization, the high rate of outpatient no-shows, non-adherence when in treatment, non-reimbursed time for prior authorizations (with nonMDs), and feeling at higher risk liability-wise with refusal by caseworkers and judges to give consent for psychotropics. Local pediatricians and family practitioners have complained they end up treating these patients without psychiatric consultation or support, and are very uncomfortable doing so.
11	Diagnosis using the DSM has its limitations, but is still a tool to justify treatment strategies and communicate with other physicians, pharmacists and providers.
11	Psychosocial treatment is so important. Non-adherence with individual and family therapy is an issue. It is too bad Texas does not utilize WRAP, Family Focus (In-home and in-school supports), partial hospitalization, and residential treatment, such as Pennsylvania does. The cuts in the MHMRA budget have impeded such limited services. Changes in foster care placement, and for the general Medicaid population, changes in phone numbers and frequent moves make it difficult to provide these services to the patient and the families.

12	A medical home through an EMR to capture as much data as possible (i.e., previous diagnoses and prescriptions) would be an ideal. To allow the PCP access to all the records including the specialists' treatment, whether it be the psychiatrist, the allergist, etc., is so needed.
	Ongoing studies adding to the evidence-based practices are so important. I am concerned as to how research and development will be funded in the future, and how this will impact the development of guidelines.
14	Having reviewed foster care treatment plans in the past, it is curious why neurologists who prescribe 10 to 15 medications often including multiple anti-seizure meds (including multiple benzodiazepines) for a single, medically fragile child have not caught the attention in the same way as psychiatrists prescribing psychotropics have.
22	Justifying one's treatment plan is always important. Quality and safety concerns must be addressed. How to incorporate a prior authorization system that is time efficient, reimbursable, and bypasses physicians having to justify to nonMDs is needed. Potential flags are understandable, but many of the Medicaid children have complex problems and are outliers despite best practices tried. Peer review, again with reimbursement for time spent, seems appropriate. Telephone consultative support, second opinions sound interesting, but how does the government pay for it? What type of fiscal benefits and penalties can be tied to measures and goals when the children and their families are so complex, often chronic, with poor prognosis as it is? Pay for performance? Would this make psychiatrists want to treat the mild cases rather than the complex, chronic ones? Already, some of our members are complaining that their psychiatric hospitals who had authorization for days of treatment are being investigated and having to pay back money to Medicaid. How is this even possible? Why would physicians want to expose themselves to these risks?
Comments	As the new president of TSCAP, it is with a sad heart that I tell you that I no longer provide care to foster care children. When I entered private practice 6 years ago, I chose only to see foster care children with Medicaid above the age of 4, as the no-show rate of the general Medicaid population was too high, and I gave up seeing under 4 with the onset of the "red flags". I gave up seeing foster care children within 2 years, as I was unable to provide the quality of care I believed was necessary. Caseworkers withheld consent for antidepressants for children who were sexually abused and suffering with depression and PTSD, and not responding to months of therapy. A judge withdrew consent on the only 3 year-old I was talked into seeing, after I asked

	for a second opinion from another child psychiatrist and a developmental pediatrician. This child ended up throwing a shoe at the foster mother while she was driving, and they were fortunate neither was injured as she rolled her SUV. The liability was too great. The time needed to do prior authorizations and the growing restrictive formulary were not conducive in my practice setting. **Members are informing me that many Austin and San Antonio child and adolescent psychiatrists are giving up Medicaid and managed care and going to fee-for-service only. Members are asking what will happen to the MHMRA system as budgets are cut once again? What do these systems do when it appears they are operating from bare bones already? Are other systems of care such as federally qualified healthcare centers the ones which will be providing services to the most at-risk Texas citizens? Members have informed me about Lone Star Circle of Care in the Williamson and Travis counties where facilities at such places as Texas A & M Round Rock, Dell and Seton hospitals/clinics, Scott & White Pediatrics, are collaborating with the mission to provide outpatient primary care and behavioral health for Medicare, Medicaid, Chips, uninsured and underinsured patients. Is it under such organizations and other "big medicine" – based systems that physicians will have less risk, and more support, when treating the most vulnerable of children?** **Many members have expressed a desire that H.B. 2163 serve to better the treatment of foster care children, and for that matter all Texas children, with quality and safety at the forefront. They have also raised concern that more and more child and adolescent psychiatrists will choose not to treat any child with Medicaid should barriers to treatment occur.**

Name: Kate Goode
Organization: other of a child who died

Section/Page #/Line #(s) (as applicable)	Comment
	My son, age 14, was prescribed Zoloft on September 12, 2009 for anxiety and very slight obsessive compulsive disorder. The diagnosis was made and the medicine ordered within five minutes of walking in the child psychiatrists office. Eight days later, after a happy day, after texting lots of friends—including a new girlfriend—and making plans for the next day at school with people, completing his homework—he hung himself in his closet. We have never heard from the doctor. We believe VERY STONGLY that the child died because of the medicine. He was a good student, had lots of friends, played freshman football at Austin High. The doctor told us there was "no risk" because he clearly was not at all depressed." This story needs to me widely known.

Dear Sir/Madame:

I have been asked, as the Medical Director for Children's Mental Health Services at the Center for Health Care Services (CHCS) in San Antonio, to give some feedback on the policy statement regarding the use of antipsychotic medications in children in the foster care system.

Basically, the recommendations appear very reasonable and they pretty much parallel the recommendations of the American Academy of Child and Adolescent Psychiatry (AACAP) in terms of the requirement of appropriate medical and psychiatric evaluation and documentation of the diagnosis, specific problem list of target symptoms, and use of monotherapy unless a rationale in extenuating circumstances is documented.

The additional concerns of antipsychotic use in preschool age children as outlined in the policy statement again the protocols outlined by AACAP - requirements for initial behavioral management, and careful documentation demonstrating clinical evaluation and evidence of having reviewed behavioral interventions first before any consideration of the use of a medication. Frequent and regular review of the response of target symptoms, being aware of possibly complicating developmental and environmental factors, and regular evaluation of the child to see if the doses can be tapered or discontinued safely, all are important considerations that have been addressed in this statement. Repeated and regular clinical evaluation to review for the accuracy of diagnosis with additional information is important a well.

The only issue in the statement with which I would disagree, based on a 20-year experience in this area, and having served on the AACAP Committee for Community Mental Health Care Services for several years, is the idea that primary care providers will be involved in the process of evaluating or treating these disorders in children, or utilizing these medications.

I have yet to find any pediatrician in the San Antonio area to whom I would like to return a patient they had referred to the CHCS, who has felt comfortable even managing a completely stabilized child for continued stimulant treatment for ADHD. They also are reluctant to screen their patients for mental health disorders. They generally do not actually "refer" or consult with us directly, but generally tell their patients, "This is a mental health problem. You really need to go find a psychiatrist."

Pediatricians and family physicians definitely refuse to treat children with mood or psychotic disorders, or to use any medication besides stimulants. This is understandable, as there are frequently so many attending complications with school, family, social issues, as well as the need to have worked with children and neuroleptics to feel comfortable in a busy q10-minute office practice.

Thus, I'm not sure if you are not boxing yourself into a corner, so to speak, to express the expectation that the involvement of primary care physicians will be a meaningful part of the plan to provide these services for children in the foster care system, if you cannot expect for this to happen in reality.

Otherwise, the policy statement reflects a lot of hard work, careful research of the literature and of the recommendations of the child psychiatry community, and I do not find that its recommendations would change what I do every day in practice. Thanks for your work on this.

Sincerely,

Thomas Hardaway, II, M.D.
Medical Director for Children's Mental Health Services
Center for Health Care Services
711 E. Josephine
San Antonio, TX 78208

From: Mike Imken
Sent: Wednesday, September 22, 2010 1:19 PM

Please see the attached comment to HB 2163.

I encourage the Texas Health and Human Services department to fully investigate the reports on antipsychotic and atypical antipsychotic medications for the sake of Texas foster children and public health and safety, particularly those reports filed within the U.S. FDA's Medwatch program -- http://www.cchrint.org/psychdrugdangers/medwatch_psych_drug_adverse_reactions.php.

Regards,
Mike Imken

Name: Error! Reference source not found., MD
Organization: former professor of child psychiatry at LSU Medical School New Orleans and SUNY Upstate Medical University, consultant to the Department of Health and Human Services, State of Alaska to develop a policy on psychiatric medication for children in state care.

Section/Page #/Line #(s) (as applicable) All comments refer to appendix A Psychotropic Medication Utilization Parameters for Foster Children	Comment
Page 3 column 3 2nd paragraph	This is a misrepresentation of what off label and non-approval by the FDA really signifies. Most medications that are not FDA approved for an indication in a specific age group have either not been studied so there is no known benefit to outweigh the known risks, or the drug company has conducted the research and it was not favorable so it was buried or the drug company asked for a new indication and submitted the data to the FDA which has turned it down because their expert panel deemed the risks out weigh the benefits so in general when one prescribes a medication for a non approved indication there is little to no benefit, the medication is no better than placebo or the risk is significant. In many cases the use of such a medication is experimental. If there was adequate research to support the off label use and safety, the drug company would have submitted the data for FDA approval and the FDA would have approved it for the new indication. Furthermore expert clinical experience is merely opinion and varies with the membership of the panel. Many experts clearly believe that the use of medication especially the anti-psychotics in children in general and foster children in particular is quite excessive, mostly used to control behavior and anger that is non life threatening albeit highly problematic and bothersome to the adults who have to deal with these children. I recommend that this section be revised to more accurately reflect the FDA's role and the significance of a medication not being FDA approved and being used

	off label.
Page 3 column 3 top	**Although these are guidelines for treating foster children, this is the only paragraph in the document that discusses specific issues of foster care. These guidelines are exactly the same as those for children in general except for this paragraph. Missing is the statistic from the 16 state Medicaid study which Texas participated in and is appendix H2 in the draft bill. On page 16 it states,** "Thirteen States were able to report on their foster care populations. In this population in 2007, the rate of AP medication use was higher at 12.37 percent, in contrast to the 1.40 percent rate for children not in foster care (Table 2)." The use of anti-psychotics is 8 times higher than in the general Medicaid population. This is clear evidence that foster children are over medicated. It is impossible that the increased incidence of schizophrenia, bipolar disorder or autism could account for an 8-fold increase in anti-psychotic medication. Clearly the increased use of medication can only be due to the use of the medication for behavior. I recommend that the discussion of use of medication in foster children clearly document that anti-psychotic medication is heavily used and over used in foster children off label and predominantly to control behavior.
Page 5 therapeutic controversies/ antipsychotics	**The guideline mentions the study comparing first and second-generation anti-psychotics but misrepresents the results. Although it is true that the medications were equally efficacious, the guidelines leave out the other part of the study showing clinically significant and worrisome side effects and although the guideline says the study cannot be extrapolated to behavior disorders, the authors of the study reach the exact opposite conclusion that the use of anti-psychotics to treat behavior given the side effects is of major concern. The abstract of the study is below so that you can draw your own conclusions.** Double-Blind Comparison of First- and Second-Generation Antipsychotics in Early-Onset Schizophrenia and Schizo-affective Disorder: Findings From the Treatment of Early-Onset Schizophrenia Spectrum Disorders (TEOSS) Study

	Linmarie Sikich, M.D., Jean A. Frazier, M.D., Jon McClellan, M.D., Robert L. Findling, M.D., Benedetto Vitiello, M.D., Louise Ritz, M.B.A., Denisse Ambler, M.D., Madeline Puglia, B.A., Ann E. Maloney, M.D., Emily Michael, B.A., Sandra De Jong, M.D., Karen Slifka, R.N., C.S., Nancy Noyes, C.P.N.P., C.S., Stefanie Hlastala, Ph.D., Leslie Pierson, M.P.H., Nora K. McNamara, M.D., Denise Delporto-Bedoya, M.A., Robert Anderson, B.S., Robert M. Hamer, Ph.D., and Jeffrey A. Lieberman, M.D. Objective: Atypical (second-generation) antipsychotics are considered standard treatment for children and adolescents with early-onset schizophrenia and schizoaffective disorder. However, the superiority of second-generation antipsychotics over first-generation antipsychotics has not been demonstrated. This study compared the efficacy and safety of two second-generation antipsychotics (olanzapine and risperidone) with a first-generation antipsychotic (molindone) in the treatment of early-onset schizophrenia and schizoaffective disorder. Method: This double-blind multisite trial randomly assigned pediatric patients with early-onset schizophrenia and schizoaffective disorder to treatment with either olanzapine (2.5-20 mg/day), risperidone (0.5-6 mg/day), or molindone (10-140 mg/day, plus 1 mg/day of benztropine) for 8 weeks. The primary outcome was response to treatment, defined as a Clinical Global Impression (CGI) improvement score of 1 or 2 and 20% reduction in Positive and Negative Syndrome Scale (PANSS) total score after 8 weeks of treatment.

	Results: In total, 119 youth were randomly assigned to treatment. Of these subjects, 116 received at least one dose of treatment and thus were available for analysis. No significant differences were found among treatment groups in response rates (molindone: 50%; olanzapine: 34%; risperidone: 46%) or magnitude of symptom reduction. Olanzapine and risperidone were associated with significantly greater weight gain. Olanzapine showed the greatest risk of weight gain and significant increases in fasting cholesterol, low density lipoprotein, insulin, and liver transaminase levels. Molindone led to more self-reports of akathisia. Conclusions: Risperidone and olanzapine did not demonstrate superior efficacy over molindone for treating early-onset schizophrenia and schizoaffective disorder. Adverse effects were frequent but differed among medications. The results question the nearly exclusive use of second-generation antipsychotics to treat early-onset schizophrenia and schizoaffective disorder. The safety findings related to weight gain and metabolic problems raise important public health concerns, given the widespread use of second-generation antipsychotics in youth for nonpsychotic disorders. Posing the controversy as anti-psychotic selection, should we use first generation vs. second generation, misses the point. The real controversy is should we be using second-generation anti-psychotics off label to treat behavior in foster children given the lack of proven benefit weighed against the known significant risk.

	I recommend that a section be added with a detailed discussion of the controversy over whether anti-psychotic medication should be used as it currently is in clinical practice given the lack of proven benefit weighed against known significant risks for the off label and predominant use of the second generation anti-psychotics.
Page 5 antipsychotic selection second paragraph	**Side effects are minimized. Weight gain is mentioned but in a way that makes it appear less significant. A weight gain expressed in kilograms such as 6.1 kg for Seroquel seems less that if expressed in lbs which would be 13.4 lbs. Also absolute weight gain doesn't capture the significance of weight gain in children since their original weights are on average much less than that of adults. An average weight gain in children of 13 lbs would be equivalent to an average weight gain in adults of 25 - 30 lbs. Very few adults would agree to take a medication for a non life threatening condition if they new that on average the medication would make them gain this amount of weight. The weight gain is significant and as mentioned above raises an important public health concern. In addition as stated in the guideline that much of anti-psychotic use of off label which means that there is no known benefit, it is very unclear how anyone can conclude that the benefit outweighs the risk when the medication is used in over 12% of foster children mainly off label to treat behavior. Even more troubling is the fact that in the discussion of side effects in this section there is absolutely no mention of the increased risk of developing type 2 diabetes or the risk of abnormal levels of prolactin which puts the child at increased future risk for osteopenia or osteoporosis and fertility problems. There is also no mention of sedation, which is a significant problem with serious implications for the child's future. The average foster child is already 2-3 grade levels behind. If given a sedating drug his or her ability to learn in school is further compromised. Any medication that compromises a child's ability to make school progress seriously decreases the child's chance of becoming a fully functioning adult. So in essence in off label use of anti-psychotic medication we are sacrificing the child's long term well being which is highly dependent on education for the short-term benefit at best if the unproven off label medication actually works of behavioral control. Although there is mention of elevated cholesterol and**

	triglycerides, the increased risk for future development of vascular and heart disease due to the elevations is not mentioned. If there is a full discussion of risks and there long term implications, the weighing of risks vs. benefits especially in off label use would be unfavorable. **I recommend that the document be revised as indicated above to include a more complete discussion of side effects and the long-term implications to the child's future well being of known side effects and risks.**
Page 2 column 1 paragraph 3	**The guideline states that a dsm 4 dx should be made prior to prescribing. Although it is true that anti-psychotic medication is approved for childhood bipolar disorder, the guidelines ignore the controversy and clear evidence that bipolar disorder is over diagnosed in children. A large number of children are diagnosed with this disorder and thereby placed on anti-psychotic medication with the belief that the proven benefits out weigh the risks but many if not most of these children do not strictly meet the dsm criteria for the disorder** (Parens E, Johnston J. Controversies concerning the diagnosis and treatment of bipolar disorder in children. *Child Adolesc Psychiatry Ment Health.* 2010;4:9.) If the children in fact are misdiagnosed and do not really suffer from bipolar disorder then the use of anti-psychotic medication for these children is actually off label, there is no proven benefit of the medication making it highly likely that the risks outweigh the benefits. Furthermore the diagnosis of bipolar disorder in children is so controversial that the American Psychiatric Association workgroup on childhood disorders and a second workgroup on mood disorders, clearly a panel of experts, both have proposed a new DSM 5 diagnosis "temper dysregulation disorder" instead of bipolar disorder for children who do not strictly meet the criteria for bipolar disorder. Any comprehensive guidelines about use of psychiatric medication in children would need to fully discuss how the controversy surrounding the diagnosis of bipolar disorder in children impacts the use of anti-psychotic medication in children but the proposed guidelines do not even see fit to briefly mention it. I recommend that a discussion of the controversy over the diagnosis of bipolar disorder and the implication of misdiagnosis and over diagnosis of this disorder

	leading to the skyrocketing use of anti-psychotic medication in foster children be added.
Page 4 column 2 paragraph 2	**This paragraph discusses informed consent. However since the guidelines are specifically relating to foster children, it is surprising that the special issues in informed consent specific to foster children are not discussed. Although an individual making treatment decisions for themselves or for their children have the right to assume significant risk if they believe that the benefit of treatment outweighs the risks, a government case worker or child welfare commissioner must place the emphasis in weighing risk vs. benefit on protecting the foster child and therefore draw a much higher threshold for assuming risk. Public officials responsible for the well being of foster children cannot assume the risk for the increased probability of long term disabling diseases such as type 2 diabetes or the long term health implications of children who are allowed to gain significant weight or increase of their blood fats or prolactin. Especially given the lack of proven effectiveness of anti-psychotic medications used off label vs. the known side effects and their long term implications, a human service commissioner or designee should not give consent with such a questionable risk to benefit ratio.** **I recommend that the commissioner of HHSC or designee review and make the decision on all requests for anti-psychotic medications for children in state custody.**
Page 8 #1	**Given the known misdiagnosis and over diagnosis of bipolar disorder as discussed above and the common off label use of anti-psychotic medication to treat ADHD, conduct disorder, oppositional defiant disorder and other behavior problems coupled with the lack of meaningful evidence of effectiveness and the significant risks, I recommend that all use of anti-psychotic medications should be reviewed even if there is an evaluation and dsm diagnosis in the record.**
Page 8 #2	**There is no scientific evidence for drawing the line at 5 or more medications. This is purely an opinion. There is no evidence of safety or efficacy for these cocktails of medicines. We know that mixtures of uppers and downers put individuals at risk and can result in death as in the cases of Michael Jackson, Marilyn Monroe, Rebecca Riley, the 4 year old in Boston and Gabriel**

	Meyers is foster child in Florida. To allow a foster child to be on 5 medications given what we know about the significant risks before the case is reviewed is to abdicate government's responsibility to protect foster children. **I recommend that review should occur on any foster child who is on 3 or more medications.**
Pages 3-4	**The general principles stated in the introduction are accepted guidelines that have been promulgated for over a decade. However there is little evidence that they are working in reducing the over usage of psychiatric medication in children in general and foster children in particular. If physician practice was actually changing due to psychiatrists following these well-established principles, the use on anti=psychotic medications especially off label use would not be skyrocketing. There would not be the frequent newspaper exposes or law-suits and the state of Texas would not be studying the problem today. Therefore any approach to reducing the overuse of psychiatric medications especially anti-psychotic medication used off label with little benefit and significant risk cannot rely on physicians or issuing new practice guidelines. The responsibility to reduce medications for foster kids lies with human services commissioners and their staffs developing policies to protect children and not signing consent for medications used off label where the risk outweighs the benefit. The consent function cannot be assigned to the parents of foster children since most consent documents are inadequate, exaggerating benefit, minimizing risk, ignoring black box warning, ignoring the benefits of non medical psycho social interventions that have proven efficacy and not providing alternatives. Also it is well known that parents feel coerced into signing consent. If they refuse they are deemed uncooperative, accused of medical neglect resulting in a possible delay of the return of their child. Again only the government child welfare caseworker and the human service commissioner can ensure that medications are used appropriately and that foster children receive the protection from unnecessary harm that they deserve.** **I recommend that HHSC develop a set of policies for informed consent, evaluating requests especially for off label medication use, and monitoring of significant side effects for the children in their care.**

Name: Debra Atkisson Kowalski, M.D.
Organization: TSPP, Chair of Child and Adolescent Committee

Section/Page #/Line #(s) (as applicable)	Comment
P4, lines 31-34	Appreciate the emphasis that off-label prescribing is the norm in pediatric care and that this is not different in psychiatry.
P 5, lines 6 - 11	Concerns about obesity, metabolic syndrome, and later heart disease and diabetes is highlighted here. As a Medical Director of a day treatment program which serves children and adolescents, including Medicaid and foster care children, I spent the last year monitoring use of these medications in our population. The highest failure mode for safe prescribing of these medications was due to parents not taking the children to the laboratory to obtain appropriate lab values. Even when our facility bought a cardiocheck and offered triglyceride, cholesterol, and glucose monitoring on-site, the parents would not send the children in a fasting state for us to obtain labs. This occurred in spite of parental education, written materials being distributed, etc. A major clinical concern I have is that lack of parental or guardian compliance in working with the physician may increase the risk to the child of taking these medications.
P 8, lines 38-40	A recommendation to facilitate consultation for non-psychiatrists serving Medicaid youth with mental health disorders is an outstanding idea. The model which Dr. Pliszka designed and helped implement with integration of mental health practicioners into pediatric clinics with a child psychiatrist as a back-up gives a model. This would help bring more psychosocial services to this population as well.
P 24, lines 6 - 15	Discusses how many children in State Medicaid programs do not get regular glucose and lipid screening; as I mentioned above, this could be due to parental noncompliance.
p. 52, lines 29 - 35	Discusses how a prior authorization process may drive practicioners out of Medicaid and may provide barriers to treatment. I could not agree more with this statement; increasing administrative burdens upon physicians to provide care could directly result in less care being available.
General Comments	This is a thorough review of the problems with prescribing antipsychotic medication to children. A

	major problem I see in treating these children is the lack of appropriate time to treat them in psychosocial interventions either first-line, or in conjunction with antipsychotic medication. Many children benefit greatly from these medications; and we as psychiatrists need to be able to use all possible tools to help these children. However, therapy is often not given or adequate time in day treatment is not given to these children. I think that improving the availability of psychosocial interventions could be immensely helpful and should be considered.

From: Joseph McCabe
Sent: Tuesday, September 21, 2010 2:08 PM

Anyone who prescribes anti-psychotics to children ought to be arrested.All of this "off-label"prescribing,which has been getting way,way out of control ought to thoroughly & rigorously reviewed at the Federal level,not just by the FDA,but my Capitol Hill

From: Heidi Noyer
Sent: Saturday, October 02, 2010 8:21 AM

Frankly, I have seen numerous people with permanent tardive dyskinesia from psychotropic medications. Also, having done foster care, I also believe that some foster parents put children on psych meds to get more money. The system is at fault for this as well. For example, having talked with many case managers and such, what I learned is that they deny extra money for problem children unless they are on psych meds. Now this is probably not the requirement, but it is what is being done. Statements like, "No, they can not have the extra money for having a difficult child because the child isn't even on psych meds." are often heard. Unfortunately, this was said even in reference to children with diagnoses younger than five. Some foster parents who are willing to have the problematic children, but need the extra funds to be able to handle such, since they are much more expensive, don't even want to do the meds, but feel they have to in order to afford keeping the children. So, getting the people who decide which category of funds gets attached to which child to do so based upon difficulties and diagnoses and NOT whether or not they are on psych meds would inherantly get these prescriptions lessoned.

In addition, I now do medical research. And what I found out, in the giant autism recovery movement, where thousands have been recovered, and have also had diagnoses of Bipolar, Schizophrenia, ADHD, OCD, etc., they have medical problems causing their diagnoses. Treating them medically can rid symptoms and behaviors much more successfully than psychotropic medications. But, it does take a while. There are doctors in Austin, and other big cities who know how. The Neuroscensory Centers know how, and some take Medicaid.

I personally had a 5-year old foster child with Tardive Dsykinesia, and frankly, I think he would have done completely fine off of all medications. Every child is different, and each family has their own beliefs, but taking the practice of extra funds only given to those on psych meds is the only way I can think of to lower all those psych. med. prescriptions.

Feel free to ask more questions.

Heidi Noyer, MS, LPC, LCDC

Name: Steven R. Pliszka MD
Organization: TSCAP, UTHSCSA, Dept. of Psychiatry

Section/Page #/Line #(s) (as applicable)	Comment
Page 41, lines 7-13	The summary should more strongly state that the number of subjects in these comparative studies was inadequate to conclude that there is no difference between the two generations of antipsychotics. Only a very large study can do this. As it reads now, the reader might think that FGA are proven to be equally more effective
Page 45,line 40 forward	This paragraph speaks of "mood stabilizers" being used first. In fact, SGA's, due to their efficacy in mania, are mood stabilizers. I think that the argument being made here is that the older mood stabilizers (lithium, divalproex, etc) are preferred. In fact there is very limited evidence, based on RCT's, that these are effective. For instance, divalproex and trileptal failed in controlled trials. Thus most clinicians view either SGA's or a "classic" mood stabilizer" as first line. I would revise this paragraph accordingly.
Page 4, lines 28-30	I would add this is similar to other pediatric medications used off label, including antibiotics, seizure medications and cancer treatments. Psychotropics are not different from other medications in this regard.
General comments	At some point, it might be desirable to include a statement about the lack of intensive behavioral interventions for the medicaid population and how restrictions on inpatient length of stay may encourage increased antipsychotic use due to the need to stabilize a child quickly

Name: Robert Rosenheck MD
Organization: Professor of Psychiatry, Epidemiology and Public Health and at the Child Study Center, Yale Medical School (Robert.Rosenheck@yale.edu)

Robert Rosenheck has received research support from Eli Lilly, Janssen Pharmaceutica, Astra-Zeneca and Wyeth Pharmaceuticals. He has been a consultant to GlaxoSmithKline, Bristol Myers Squibb, Organon and Janssen Pharmaceutica. He provided expert testimony for the plaintiffs in UFCW Local 1776 and Participating Employers Health and Welfare Fund, et al. v. Eli Lilly and Company; for the respondent in Eli Lilly Canada Inc vs Novapharm Ltd and Minister of Health, respondent; for the Patent Medicines Prices Review Board Canada, in the matter of Janssen Ortho Inc. and "Risperdal Consta" and is testifying expert for the State of Texas.

Section/Page #/Line #(s) (as applicable)	Comment
Appendix A, p. 5 line 23 ff (Antipsychotic Selection)	**This section is vague and fails to point out that there are virtually no effectiveness studies of antipsychotics in child or adolescent patients described in this document as having the most common disorders among Foster Care clients in Texas: i.e. those with externalizing disorders such as conduct disorder or oppositional defiant disorder.**
Appendix A, p. 5 line 34.	**The statement that there is "best evidence with ripseridone" is misleading in that it suggests risperidone may be the best drug. Risperidone is the only drug with FDA approval for autism, which is not listed as one of the disorders occurring with any frequency in foster care settings in Texas, but evidence for benefits of risperidone in the disorders listed above, as most common in Texas Foster care programs, is as limited as for any other antipsychotic drug. Studies of risperidone have focused on schizophrenia, bipolar disorder and ADHD in low IQ children, but not in the most common disorders in Texas Foster care as presented in** Appendix B - Use of Psychoactive Medication in Texas Foster Children.
Appendix A, P. 5 line 34	There is no mention of the fact that risperidone has the highest risk of prolactinemia and concomitant syndromes such as gynecomastia which makes it highly doubtful that it could be considered the best drug for this population.
Appendix A, p. 5, col 3, line 1ff	The statements about weight gain state that there is great variability in weight effects of SGAs, but it is clear from the data presented that all of the SGAs cause substantial weight gain in children. The presentation of data in kilograms may tend to minimize the magnitude of this risk for readers more

	used to seeing data in pounds.
Appendix A, p. 5, col 3, line 14 ff	Assertions are casually made about higher risks of TD without citation for FGAs in children and adolescents. However the most recent comprehensive review by Correl (2008), not cited in the bibliography, found a rate in pediatric cases of only 0.4% in a large sample and noted that firm conclusions about TD risk were precluded. This section thus seems unduly biased in favor of SGAs, where serious metabolic risks are well documented and severe, but where neurological side effects in children and adolescents with FGAs are far less well documented. The review seems further unduly biased in favor of risperidone, in particular, which may have been studied more extensively than other drugs, especially in autism (which does not occur in Texas Foster Care with any frequency) but has not been shown to be superior to other drugs. In fact the most serious and unique hazard associated with risperidone, prolactinemia is not acknowledged at all. The report should be more balanced acknowledging the lack of good information on all of these drugs in children and adolescents and especially for the diagnostic problems most common in Foster Care in Texas particular.

Name: Laurie Seremetis, MD, MPAff
Organization: Community Psychiatrist, Austin TX

Section/Page #/Line #(s) (as applicable)	Comment
Summary & Findings, p.4, lines 12-15: "Treatment guidelines…after psychosocial interventions have been shown to be insufficiently effective…"	This study does not address the paucity of psychosocial interventions covered by or available to Medicaid recipients. Nor does it address the characteristics of children and families who are more likely to receive antipsychotics outside of treatment guidelines or fail to receive appropriate psychosocial interventions. Until these are addressed, high risk and high need children on Medicaid will continue to receive inappropriate, primarily medication-based treatment.

From: Duane Sherry
Sent: Thursday, September 16, 2010 8:57 PM

Children in Texas need our protection, especially those who are in Medicaid or Foster Care programs.

The drug makers have targeted these vulnerable groups for years, without regard to the injury and premature death that comes from the use of psychiatric drugs with children and youth.

Psychiatrist Peter Breggin, M.D.(former teaching professor at Harvard Medical, consultant to the National Institutes of Mental Health, aka "the conscience of psychiatry") gets right to the point in his research.... A must-read for anyone involved in legislation in this area -

http://breggin.com/index.php?option=com_content&task=view&id=38

The Alliance for Human Research Protection has several articles on the dangers of these drugs for children and youth. Vera Sharav has chronicled these articles for years, after losing her own son to these drugs -

http://www.ahrp.org/cms/content/blogsection/5/52/

We have an opportunity in Texas... to lead, by example...
To say "no" to the pharmaceutical industry when it comes to mind-altering, brain-damaging, body-injurying, spirit-numbing drugs for kids... ."No."

And "yes" to safer, more effective options -

http://discoverandrecover.wordpress.com/wellness/

Passionately,

Duane Sherry, M.S.

Name: Claudia Smith
Organization: Citizens Commission on Human Rights

Section/Page #/Line #(s) (as applicable)	Comment
	In response to the draft HB2163 study, we would again direct your attention to our previously submitted references and independent studies and statistics. There you will find much evidence requiring caution in using psychotropic drugs on children and data that supports the wisdom of prior authorization before prescribing or the eventual implementation of a reduction of such prescriptions. One such caution is from the FDA's Director of the Division of Psychiatric Products who asserts that using these proposed drugs is considered a significant risk because all of the long term adverse effects on children are not fully known, because of the possible adverse effects on growth and development and because the known adverse physical side effects can be permanent, i.e., acute extrapyramidal symptoms and tardive dyskinesia. While we object to the bulk of this report as a very generalized defense of questionable psychiatric practices, the report does confirm our concerns and those of most who testified in favor of HB2163. According to this report Texas children under the age of 6 are getting strong, expensive antipsychotic drugs even though there is little to no strong evidence to support such use. Such usage escalated in the state of Texas between 2003-2007, as reported by HHSC statistics, to roughly $297million in spending. The fact that this problem has continued to grow this many years after the HHSC Inspector General investigation illustrates a lack of dedication to solving this problem that will only be solved through legislative action. The problem of young children being drugged with potent and dangerous drugs has not been missed by other states. Florida instituted a prior authorization program, which by media accounts resulted in drastic reductions in the use of these drugs in children five and under. Per the results of HB2163 study, the state of Georgia has implemented a prior authorization program that not only saved money but resulted in better patient health. According to a recent New York Times article, psychiatrists at Tulane

	University have instituted a program to help wean Medicaid children off antipsychotic drugs. While we cannot speak to the intent or methods used by those running the program, however, the basic goal of weaning children off these drugs is certainly laudable. Whether by accident or by design, the authors of this report appear to generalize the idea of safety and efficacy of these drugs to include the entire Medicaid child population. This could create a false impression that it's okay for parents or guardians to put children of any age on these drugs. While HHSC offers to educate parents and guardians, the bulk of this report, shows why this cannot be done. Parents and guardians have the right, the duty and responsibility to make medical decisions for these children and they cannot do so if they are not given an honest picture of the risks or any purported benefits, as well as all alternative treatments to drugs. This report should be pared down to just the facts. And the facts are: according to HB2163 study, "At present there are no bio-markers" for precise diagnosis of mental disorders which would put psychiatry on a par with physical medicine and considering the seriousness of the "Therapeutic Controversies" discussed, a prior authorization before prescribing dangerous drugs to young children would be implementation of a necessary oversight of an area that has been noted historically for abuse.

Name: Marsha Spalding, MD/Medical Director of Lubbock Regional MHMR Center
Organization: Lubbock Regional MHMR Center

Section/Page #/Line #(s) (as applicable)	Comment
Section 4/p.6/Lines #9-34	Excellent Summary of "What we Know"; very well written and to the point.
Section 4/p.6/Lines #36-40	Critically important issue to point out
Section 6/p.8/Lines #30-36	Very Valid Options; particularly the suggestion of extending the UR Process
Section 9/p.10/Lines #19-25	Very well written. Research and Factual based; which assists in eliminating the some of the fears and potentially overreaction created by the initial community concerns.
Section 12/p.31-32/Lines #3-37 and #39-19	Very convincing evidence for the use of Risperidone in this difficult population.
Section 27/p.25/Lines #5-18	Excellent description and definition of "Standard of Care" in regards to the use of antipsychotic medication in children
Section 27/p.25/Lines #20-39	Very well organized summary of how evidence based medicine is determined; based on valid scientific study. Easy to understand for the nonclinical reader as well.
Section 27/p.41/Line #41	Typo: "because it because there is"
Section 33/p.51/Lines #13-23	Excellent example of the need to utilize antipsychotic medication for aggression despite a formal diagnosis that might not warrant its use.

Name: Joshua Sparrow, MD, as private citizen
Credentials:
Child psychiatrist,
Director, Special Initiatives of Brazelton Touchpoints Center
Children's Hospital, Boston,
Assistant Professor Harvard Medical School

ALLCOMMENTS PERTAIN TO APPENDIX A ON PSYCHOTROPIC MEDICATION PARAMETERS

Section/Page #/Line #(s) (as applicable)	Comment
APPENDIX A	
p. 5, Therapeutic Controveries, Antipsychotic selection	The statement that the best evidence for the use of antipsychotics in children for behavioral disorders is for risperidone is unclear because it does not specify that this comparison between risperidone and other drugs is limited by how few studies in this context have been conducted for other drugs. Does "best" evidence mean here that the scientific methodology in the risperidone studies is strong and the findings solid, or simply that studies of other drugs have been done far less frequently or not at all? – see also charts on pages 16 and 17, where the caveat that prescription of typical antipsychotics should be reserved for children who have not responded to nonpharmacological interventions is not also offered for the prescription of atypical antipsychotics. This creates the impression that atypical antipsychotics might be first line treatments for behavioral problems in children, a controversial assertion that requires a reference to the evidence. Omission of citations for CATIE and CUTLASS studies showing no superiority of "2nd generation" or "atypical" antipsych; no citation for TEOSS study involving children although mention of molindone here probably comes from that study. Note that molindone is out of patent and no longer manufactured, in all likelihood because of aggressive marketing of atypicals. It is less likely to cause obesity and metabolic syndrome than atypicals, even though atypicals have been marketed as "safer" than older drugs such as molindone; no information from TEOSS on relative disadvantages of atypicals when compared to typical antipsychotics;

	it is simply noted that the most common situations in which anti-psychotics are prescribed in children are conduct disorder and oppositional defiant disorder but no discussion ensues about why this might be and whether or not this constitutes acceptable practice and acceptable level of risk. Oppositional defiant disorder and conduct disorder are not psychotic disorders. Both are easily misdiagnosed in the context of post-traumatic stress disorders and reactive attachment disorders which are both highly likely in foster children. In addition, both involve conflict between the child and other people or the child's environment. Among the questions that need to be raised here is whether it is acceptable to be exposing foster children to the risks of antipsychotics when their problematic behavior may be signaling problems in their environment; **there is no citation for the statement that first generation antipsychotics pose a higher risk for the development of tardive dyskinesia in chronically treated individuals, and although this was an intensively marketed claim for the atypical antipsychotic, it has not been clearly established;** **there is no mention of the risk of elevated prolactin levels and galactorrhea with atypical antipsychotics, despite the fact that this serious side effect is more common with some atypicals than with some typical antipsychotics – see also charts on page 16 and 17 where hyperprolactinemia is mentioned for certain typicals but is omitted for atypicals;**
p. 9	**Omission of disclosure of conflicts of interest indicating past and current fiduciary relationships with pharmaceutical industries**

From: Nancy Wilson
Sent: Sunday, September 26, 2010 12:00 PM

I thought you might find this information helpful for your review. All best, Nancy Wilson

http://www.newswise.com/articles/psychotropic-medication-and-youth-in-foster-care-report

Comment Form
H.B. 2163 Draft Report
Appropriateness and Safety of Antipsychotic Medications for Medicaid Children Under Age 16

Name: Bruce D. Perry, M.D., Ph.D.
Organization: Senior Fellow, The ChildTrauma Academy, Houston TX; Adjunct Professor, Department of Psychiatry, Northwestern University School of Medicine, Chicago IL

Please submit comments by September 30, 2010 to lisa.kirsch@hhsc.state.tx.us or to Lisa Kirsch, Texas Health and Human Services Commission, P.O. Box 13247, Mail Code BH-4100, Austin, TX 78711

Section/Page #/Line #(s) (as applicable)	Comment: I will number my comments and outline them v briefly. I would be happy to elaborate, expand and provide v further documentation on these comments should you v wish further input. My general comments and concerns v follow: v
Appendix A: Concerns about lack of trauma-informed practice	These "guidelines" do not reflect a current understanding v of the complexity of the impact of trauma, neglect and v maltreatment on the brain. They are, simply, NOT v "trauma-informed." Understanding the complex impact of v developmental trauma on the brain is an essential issue v when thinking about psychopharmacology as the key site v of action for the majority of psychotropic medications is in v the very monoamine networks (norepinephrine, serotonin v and dopamine) that are impacted by developmental v adverse events and trauma (e.g. Perry, 2006). This means v that any of the scant reliable findings (which are very few) v on efficacy of medications in child neuropsychiatric v conditions from typical outcome studies in child/adolescent v populations can not be generalized to children in the foster v care system (a population characterized by high rates of v trauma, neglect and exposure to violence). Basically what v this means is that each child is likely to have somewhat v unique neurophysiological and neurodevelopmental v organization; this makes it highly likely that they will exhibit v idiosyncratic responses to any given medication. (This is v indeed the experience of our large clinical group – that has v seen directly or had program oversight of more than v 20,000 children in the foster care system in dozens of v

	states) This, therefore, requires individualized, empirically-x driven psychopharmacological practice. To complicate this x further, there are NO well-controlled studies that have x demonstrated efficacy for any neuropsychiatric x presentation in the foster care population. And making a x responsible choice to use medications in these children will x involve a very conservative and cautious, well-informed x process that is guided by the principles that were outlined x in Appendix A: namely a full medical work-up; engagement x in quality non-pharmacological treatment; introduction of a x single medication with clear target symptoms and a way to x measure and track these; determining efficacy or not x before switching or adding another medication (which will x require the same process). The only way to ensure that this x responsible process will be followed is to require pre-x approval and guidance in this process where all of these x factors are documented, tracked and monitored. This form x of responsible (trauma-informed) practice will not occur if x monitoring only is triggered by the extreme factors x suggested in factors for review section of Appendix A; page x 8. To institute oversight only after these extreme x situations is too little too late and will allow ongoing x irrational and harmful prescribing practices with this highly x vulnerable population. x
Appendix A: Concerns about lack of acknowledgement of vulnerability of population	These guidelines do not acknowledge the documented x physical health vulnerability of the foster care population. x Children in this group have increased risk for cardiac, x endocrine and cardiometabolic problems as they age and x become adults (e.g., Anda et al., 2006). The adverse effects x of many psychotropic medications especially antipsychotic x medications (e.g., increased wt. gain, cardiometabolic x problems, increased risk for diabetes) are well x documented. This physiologically vulnerable population is x the last group you should ever use many of these x medications on (again, especially second generation x antipsychotics) unless there are NO reasonable alternatives x and or very clear target symptoms suggestive of an x overlapping primary neuropsychiatric condition (e.g., x schizophrenia) that has been complicated by x developmental trauma. This is especially so since there has x been no demonstration of efficacy in any primary x neuropsychiatric condition in the foster care population. x
Appendix A: Concerns about lack of full	The Institute of Medicine of the National Academy of x Sciences has been so concerned about the influence of x

disclosure regarding potential conflict of interest	industry on medical practice – including the development p of guidelines such as these in discussion that they have p reviewed and made recommendations regarding p ap ropriate disclosure regarding potential conflicts of p interest (assuming that independent participants in the process cannot be engaged). (Conflict of Interest in Medical p Research, Education, and Practice, National Academy Press, p Washington DC, 2009). In brief, the current process to p derive these guidelines does not provide the independence p or disclosure that would be desirable (according to the p IOM). At a minimum, the Members of the Ad Hoc Working p Group on Psychotropic Medication Guidelines for Foster p Children should provide full public disclosure regarding p their current and past relationships with industry; including p direct funds for consultation, speaking, and indirect funds p to sup ort "education" or "research." This should also p include the professional groups who are claiming to p endorse this: disclosure of the same items for key officers p and a statement regarding what percentage of the p organizations budget is derived from industry sup ort or p industry foundation sup ort. p p
Appendix A: A general comment	Children in foster care have been taken from family and p often community into the care of the State. We make this p choice with their best interests in mind yet by making this p decision, the State agrees to stand in and serve as their p guardian. It is therefore essential that we honor this p obligation by giving the highest level of attention and p scrutiny to their medical care and insist that the level of p vigilance we would have for our very own children is provided for these vulnerable children and youth. And in p the case of taking medications we must be very aware of p the lack of scientific evidence to sup ort the use of p medications in this population and the know risks of taking p these medications seen across diagnoses and age. With p minimal expectation of positive outcome and moderate to p high risk for bad outcomes it should be with great temerity p that we agree to let "our" foster children be medicated p without a highly monitored process to ensure quality practice. p

Qualifications and Basis for Opinions

I have extensive training, research and clinical experience in the areas of child mental health, pediatric psychopharmacology and child maltreatment. In addition to my M.D., I have a Ph.D. in Pharmacology. I have taught psychopharmacology at the graduate (medical) and post-graduate level, have served on hospital pharmacy committees; I founded and ran the Pediatric Psychopharmacology Clinic at Texas Children's Hospital and In addition I have served on the pediatric psychopharmacology section of the USP Pharmacopeia. I have conducted research and published extensively in the area of childhood trauma and maltreatment (many of our patients have been and are currently in foster care). I have worked with children and youth in the foster care systems in dozens of states and have led and continue to lead a range of clinical service delivery and training projects in the child protective, juvenile justice and mental health systems in multiple states (including Illinois, Pennsylvania, New Jersey, California, Oregon, New Mexico and Alberta Canada). I have extensive first hand experience with psychopharmacology in this population (i.e., maltreated and traumatized children; children in foster care) and am also very well aware of the range of non-pharmacological interventions available for these children and youth.

REFs

Anda, R.F., Felitti, R.F., Walker, J., Whitfield, C., Bremner, D.J., Perry, B.D., Dube, S.R., j Giles, W.G. (2006) ***The enduring effects of childhood abuse and related experiences: a convergence of evidence from neurobiology and epidemiology***, European Archives of j Psychiatric and Clinical Neuroscience, 256 (3) 174 - 186,j

Perry, B.D. (2008) ***Child maltreatment: the role of abuse and neglect in developmental psychopathology*** jin jTextbook jof jChild jand jAdolescent jPsychopathology j(Theodore jP. j Beauchaine and Stephen P. Hinshaw, Eds) pp. 93-128 Wiley, New York j

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