
Working together to improve health care quality, outcomes, and affordability in Washington State.

# Pediatric Psychotropic Use Report and Recommendations

**TBD**

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## Executive Summary

The Dr. Robert Bree Collaborative was established in 2011 to provide a forum in which public and private health care stakeholders can work together to improve quality, health outcomes, and cost effectiveness of care in Washington State. Antipsychotic prescribing rates have dramatically and consistently increased for adolescents and young adults. The United States Food and Drug Administration has approved antipsychotic medications for use in children and adolescents with schizophrenia, bipolar disorder (manic/mixed) and irritability with autistic disorder. In addition to the FDA-approved indications, antipsychotics have also been found to be helpful in reducing disruptive behavior in children and adolescents *without* psychosis, allowing the child or adolescent to remain in school, in home, and enabling them to be receptive to other forms of therapy. These off-label uses of antipsychotic agents (i.e., for conditions not approved by the FDA) include aggressive, impulsive, and disruptive behaviors, often in patients with attention-deficit hyperactivity disorder (ADHD), in the absence of psychosis

Evidence shows that atypical antipsychotic use is associated with patient harms including obesity, cardiovascular effects including hypertension, the possibility of tics, and other effects on the developing brain. Additionally, long-term research on the effects of atypical antipsychotic use in youth is lacking. Evidence-based first line treatments for aggressive, impulsive, and disruptive behaviors in the absence of psychosis include psychosocial therapies. However, there is a lack of accessible and cost-effective behavioral therapy options, especially outside of urban areas and few effective alternative pharmacotherapy options available. Many patients do not receive an appropriate mental health assessment and if antipsychotics are prescribed, receive monitoring of side effects.

The Bree Collaborative elected to address this topic and convened a workgroup to develop recommendations from January 2016 to November 2016. This report aims to highlight and help facilitate adoption of evidence-based best practices in:

1. Conduct initial medical and psychological evaluation using appropriate assessment
2. Ensure that the patient and family has access to comprehensive, family-centered psychosocial care whether within the primary care setting through integrated behavioral health care or through a supported referral
3. Use evidence-based, best practice antipsychotic prescribing recommendations such as from the American Academy of Child and Adolescent Psychiatry
4. If antipsychotics are prescribed, manage side effects including monitoring for changes in weight blood glucose (HgA1C), cholesterol, and other metabolic changes (baseline and at regular intervals).

## Dr. Robert Bree Collaborative Background

The Dr. Robert Bree Collaborative was established in 2011 by Washington State House Bill 1311 *"…to provide a mechanism through which public and private health care stakeholders can work together to improve quality, health outcomes, and cost effectiveness of care in Washington State."* The Bree Collaborative was modeled after the Washington State Advanced Imaging Management (AIM) project and named in memory of Dr. Robert Bree, a pioneer in the imaging field and a key member of the AIM project.

Members are appointed by the Washington State Governor and include public health care purchasers for Washington State, private health care purchasers (employers and union trusts), health plans, physicians and other health care providers, hospitals, and quality improvement organizations. The Bree Collaborative is charged with identifying up to three health care services annually that have substantial variation in practice patterns, high utilization trends in Washington State, or patient safety issues. For each health care service, the Bree Collaborative identifies and recommends best-practice evidence-based approaches that build upon existing efforts and quality improvement activities aimed at decreasing variation. In the bill, the legislature does not authorize agreements among competing health care providers or health carriers as to the price or specific level of reimbursement for health care services. Furthermore, it is not the intent of the legislature to mandate payment or coverage decisions by private health care purchasers or carriers.

See **Appendix A** for a list of current Bree Collaborative members.

Recommendations are sent to the Washington State Health Care Authority for review and approval. The Health Care Authority (HCA) oversees Washington State's largest health care purchasers, Medicaid and the Public Employees Benefits Board Program, as well as other programs. The HCA uses the recommendations to guide state purchasing for these programs. The Bree Collaborative also strives to develop recommendations to improve patient health, health care service quality, and the affordability of health care for the private sector but does not have the authority to mandate implementation of recommendations.

For more information about the Bree Collaborative, please visit: www.breecollaborative.org.

Antipsychotic prescribing rates have dramatically and consistently increased for adolescents and young adults, much of which is due to off-label use, for diagnoses not approved by the US Food and Drug Administration. Patients are not provided access to psychosocial services as a first line treatment and monitoring of side effects is rare. The Bree Collaborative elected to address this topic and convened a workgroup to develop recommendations from January 2016 to November 2016.

See **Appendix B** for the Pediatric Psychotropic Use workgroup charter and a list of members.

## Problem Statement

The United States Food and Drug Administration (FDA) has approved antipsychotic medications for use in children and adolescents with schizophrenia, bipolar disorder (manic/mixed) and irritability with autistic disorder. In addition to the FDA-approved indications, antipsychotics have also been found to be helpful in reducing disruptive behavior in children and adolescents *without* psychosis, allowing the child or adolescent to remain in school, in home, and enabling them to be receptive to other forms of therapy. These off-label uses of antipsychotic agents (i.e., for conditions not approved by the FDA) include aggressive, impulsive, and disruptive behaviors, often in patients with attention-deficit hyperactivity disorder (ADHD), in the absence of psychosis.[1]

Prescribing rates have dramatically and consistently increased for adolescents and young adults, especially for those diagnosed with ADHD.[2] Nationally, between 2002 and 2007, there was a 62% increase in antipsychotic use among children enrolled in Medicaid.[3] Recent research has shown the rate of growth to have tapered off after 2008, but not to have decreased.[4] These high numbers of prescriptions are problematic and potentially harmful as increasing evidence shows that atypical antipsychotic use is associated with patient harms including obesity, cardiovascular effects including hypertension, the possibility of tics, and other effects on the developing brain.[5] Additionally, long-term research on the effects of atypical antipsychotic use in youth is lacking.

Evidence-based first line treatments for aggressive, impulsive, and disruptive behaviors in the absence of psychosis include psychosocial therapies. However, there is a lack of accessible and cost-effective behavioral therapy options, especially outside of urban areas and few effective alternative pharmacotherapy options available. The combination of high impact symptoms and poor access to non-pharmacologic treatments can lead providers to prescribe antipsychotic agents for these off-label uses. The expansion in use of antipsychotics outside of patients with psychosis is partly due to the introduction of second-generation or atypical antipsychotics that were first purported to have a lower risk of certain side effects such as tardive dyskinesia, an involuntary movement disorder that can become permanent, than found with first generation or typical antipsychotics.[6]

Washington State has a gap between evidence-based practices, patient-centered care and common practice for children under 21 diagnosed with aggressive, impulsive, and disruptive behaviors in the absence of psychosis. Many do not receive a validated mental health assessment or a referral to psychosocial care as the first-line intervention nor monitoring of symptoms, and if antipsychotics are prescribed, monitoring of side effects. However, Washington State has also made advances such as in funding the Partnership Access Line, a telephone-based child mental health consultation system for primary care providers. Furthermore the recommendations of this workgroup are supported by changes to the Healthcare Effectiveness Data and Information Set (HEDIS) which now includes metabolic monitoring, avoiding multiple antipsychotic prescriptions, and access to psychosocial or behavioral health care for children and adolescents who have been prescribed an antipsychotic.

## Focus Areas and Goals

For children and adolescents under age 21 without a diagnosis of an FDA-approved indication for antipsychotic prescribing (i.e., schizophrenia, bipolar I disorder: manic or mixed, and irritability with autism spectrum disorder).

1. Conduct initial medical and psychological evaluation using appropriate assessment
2. Ensure that the patient and family has access to comprehensive, family-centered psychosocial care whether within the primary care setting through integrated behavioral health care or through a supported referral
3. Use evidence-based, best practice antipsychotic prescribing recommendations such as from the American Academy of Child and Adolescent Psychiatry
4. If antipsychotics are prescribed, manage side effects including monitoring for changes in weight blood glucose (HgA1C), cholesterol, and other metabolic changes (baseline and at regular intervals).

## Glossary

**Antipsychotic Medications**: A group of psychotropic medications approved by the U.S. Food and Drug Administration for the treatment of schizophrenia, bipolar disorder, and irritability associated with autism. Antipsychotics are divided into first generation or typical, developed in the 1950s, and second generation or atypical antipsychotics developed in the 1980s. Second generation antipsychotics include aripiprazole, asenapine, clozapine, iloperidone, olanzapine, paliperidone, quetiapine, risperidone, and ziprasidone and are often prescribed for other diagnosis than those approved by the FDA.

> **More information**: Agency for Healthcare Research and Quality http://effectivehealthcare.ahrq.gov/index.cfm/search-for-guides-reviews-and-reports/?productid=786&pageaction=displayproduct

**Behavioral Health**: Encompassing both mental health care and substance use treatment, behavioral health is care meant to address health behavioral, life stressors and crises, stress-related physical symptoms, and other patient needs.

**Psychosocial Treatments**: A broad category of behavioral health interventions that includes behavioral management along with social and vocational training and teach skills important to helping children, adolescents, and their families learn necessary skills.

## Stakeholder Actions and Quality Improvement Strategies

These recommendations should not take the place of clinical advice.

**Table 1: Summary of Stakeholder Recommendations**

| | Medical Evaluation | Psychosocial Interventions | Considering Antipsychotic Medication | Monitoring Effectiveness and Side Effects | Interacting with schools |
|---|---|---|---|---|---|
| **Parents and Caregivers** | Address concerns with primary care provider | Participate in the intervention and coordinate care with the primary care provider | Prepare questions and engage in shared decision making with provider | Talk about concerns with your provider and monitor for side effects | Advocate within the school system as needed |
| **Primary Care Providers (including Pediatricians) and Specialty Prescribing Providers** | Conduct comprehensive evaluation | Facilitate access to evidence-based therapy via integrated behavioral health or through a referral with a warm hand off | Work with the parent or caregiver to reach a decision together | Conduct baseline and regular monitoring of side-effects and reassess the need for antipsychotics | Support the parent or caregiver as needed |
| **Behavioral Health Care Providers (Prescribers and Non-prescribers)** | Communicate with primary care provider | Use evidence-based psychosocial interventions appropriate for the diagnoses | Continue to offer psychosocial services | Regularly monitor the effect of psychosocial interventions to ensure efficacy | Support the parent or caregiver as needed |
| **Commercial and Medicaid Managed Health Plans** | Cover mental health consultation services | Ensure adequacy of behavioral health network | Facilitate second opinion programs such as the Partnership Access Line | Track appropriate use and management using 2015 HEDIS definitions | n/a |

### For all Stakeholders

- Review the Agency for Health Care Research and Quality's information on first and second generation antipsychotics for children and young adults here: https://effectivehealthcare.ahrq.gov/ehc/products/150/2061/atypical-antipsychotics-off-label-update-surveillance-160705.pdf

### Parents and Caregivers

**Note:** We use "child" to refer to a child/adolescent or dependent under 21 including foster children and grandchildren or others who may be under your care.

- Medical Evaluation
    - Contact your child's primary care provider with your concerns and schedule an appointment to address them
    - Because of the nature of the evaluation, one or more visits may be necessary to complete a comprehensive health review before proceeding with a recommended plan of care
    - Discuss appropriate psychosocial interventions, like family therapy, with your child's primary care provider.
    - Access resources and reach out to community groups aimed at parents. Refer to **Appendix F**.
- Psychosocial Interventions
    - Ask your primary care provider or care team about how to find psychosocial interventions and look for providers in your area. These might include:
        - Family therapy, problem solving therapy, multisystemic therapy, social skills training, parent child interaction training (PCIT), and others
        - Sources of information (i.e. primary care provider, school, web resources).
    - Research shows that parent or caregiver involvement is the biggest predictor of a successful psychosocial intervention. If psychosocial interventions are offered, be sure that you as the parent or caregiver are part of the treatment.
    - Work to coordinate your child's care with your primary care provider.
- Considering Antipsychotic Medication
    - Ask your provider to include you and your child in decisions about whether to use antipsychotic medication. This can be done through shared decision making with a patient decision aid – these are tools that help people talk about harms, benefits, and questions around health care issues.
    - Prepare a list of questions to ask your child or dependent's clinician in advance of an appointment. There are many high-quality lists of questions. We recommend the Agency for Healthcare Research and Quality's *Antipsychotic Medicines for Children and Teens A Review of the Research for Parents and Caregivers* questions below: [7]
        - How well medicines other than antipsychotics might work to help your child's symptoms.

        - What non-medicine treatment options are available, such as psychosocial interventions, and if they might help your child.
        - The benefits of taking an antipsychotic or adding one to treatment.
        - Which antipsychotic medicine might work best for your child based on his or her age and condition.
        - The possible side effects from taking an antipsychotic, especially weight gain, drowsiness, and uncontrollable movements like tics and tremors.
        - The risk for a serious side effect.
        - Ways to help you notice side effects so they can be treated or so the medicine can be changed.
        - Which treatment option best fits your likes, dislikes, and values.
        - The cost of each medicine.
        - What symptoms the medication is targeting.
- Monitoring Effectiveness and Side Effects
    - Antipsychotic medications can have serious side effects which include weight gain, increased blood glucose (sugar) and insulin levels, elevated blood cholesterol and/or triglyceride levels, altered prolactin and thyroid hormone levels and involuntary movements such as tics and tremors. These are only possible side effects and may not occur in your child.
    - Let your child's primary care provider know of any family history of obesity, diabetes, abnormal cholesterol (dyslipidemia), high blood pressure (hypertension), or heart disease.
    - It is important to watch for rapid weight gain or an increase in any of the following: drowsiness, appetite, urination, or thirst and to talk to your child about these side effects. Though much less common, involuntary movements are a reason to call your doctor right away. If you or your child experience a drug-related side effect, contact the prescribing physician. Antipsychotic medications should not be abruptly discontinued.
    - Your primary care provider should measure your child or dependent's weight, height, blood sugar, and cholesterol before he or she starts any antipsychotic medication. This blood work at the beginning of treatment and then at regular intervals is needed to monitor for metabolic side effects. Blood work should include testing blood glucose, cholesterol, and triglyceride levels. How often this monitoring is conducted will depend on the status of your child's disorder, side effects your child may be experiencing, and for how long your child has taken the medication.
    - Frequent follow up visits with the treating physician will be necessary to evaluate for effectiveness of antipsychotic medications, side effects related to movement disorders and monitoring of weight, blood pressure and blood work. Early identification of side effects related to the use of antipsychotic medications may help decrease the severity of these side effects and prevent long-term complications.

    - Typical frequency of visits after starting treatment is 4 weeks, 8 weeks, 12 weeks and then every 3 months for one year, every 6 months after the first year. Additional visits may be necessary at the discretion of the treating physician
    - It is important to reassess the effect of medication on symptoms, side effects and the need for ongoing medication, every 6-12 months, with your child's physician, after starting treatment with antipsychotic medications.
- Interacting with Schools
    - Review resources for parents: www.k12.wa.us/SpecialEd/Families/default.aspx and on page 15.
    - If you are concerned about your child, make a request for educational accommodations also known as a 504 plan (to lead to an Individual Education Plan or IEP) in writing. The Federal Individuals with Disabilities Education Act (IDEA) mandates that school districts identify and evaluate children with disabilities, regardless of severity, up to age 21.
    - Review the Department of Education's steps to ensure that your child has an educational plan centered around them in **Table 5: Special Education Steps under IDEA** (page 17)
    - Look for an advocate in your child or dependent's school, such as the school psychologist, a teacher, counselor, or the principal.
    - Get the information you need about advocating for your child in the school system. A list is available on page 15.

### Primary Care Providers (including Pediatricians) and Specialty Prescribing Providers (e.g., Psychiatrist)

**Note:** These recommendations are for non-FDA approved use of antipsychotics in children without schizophrenia, bipolar I disorder: manic or mixed, and irritability with autism spectrum disorder.

- Medical Evaluation
    - Conduct a comprehensive medical examination prior to considering a diagnosis (e.g., hearing and vision screening, considering the side effects of other medication on the patient's behavior, ruling out other diagnoses)
    - Examine pediatric patients in the context of their whole family dynamic.
    - Consider learning disabilities or developmental problems.
    - Consider autism spectrum diagnosis.
    - Patients should be evaluated using a Diagnostic and Statistical Manual of Mental Disorders (DSM) validated behavior checklist (e.g., Vanderbilt Assessment Scale) to help assess possible causes of disruptive behavior or other behavioral health condition(s) and for possible comorbidities and other problems.
    - For patients with other behavioral health conditions, primary medications (e.g., stimulants, antidepressants) should be tried and dose optimized as necessary prior to prescribing antipsychotics.

- Consider calling the Partnership Access Line for questions about evaluation. More information on this service is available here: www.seattlechildrens.org/healthcare-professionals/access-services/partnership-access-line/
- The University of Washington has a high-quality resource library of screening and surveillance tools for child and adolescent mental health available here: https://depts.washington.edu/dbpeds/Screening%20Tools/ScreeningTools.html

- Psychosocial Interventions
  - If other causes for aggressive, impulsive, and disruptive behaviors have been ruled out through a medical evaluation, provide psychosocial intervention. Ideally this would take place either internally through integrated behavioral health services or through a supported referral to external services. A supported referral should include a warm handoff to specialty behavioral health services with which the referring provider has a relationship and access to a shared care plan for individual patients with bi-directional information flow.
    - If psychosocial services are integrated into primary care, follow the recommendations for integrating behavioral health into physical health care here: www.breecollaborative.org/topic-areas/behavioral-health/, when available. Ideally, pediatric patients would be able to receive evidence-based behavioral health care within their primary care clinic that is tailored to meet their needs that includes access to psychiatric consultation both for the primary care staff and for the patient and family, either in-person or through telehealth.
  - Antipsychotic medication may not be necessary or may be minimized after effective psychosocial therapy
  - If psychosocial services are provided off-site, communicate with the psychosocial provider as for any other specialty referral
- Considering Antipsychotic Medication
  - Consider calling the Partnership Access Line for questions about prescribing antipsychotics.
  - Talk with children and their families about the harms, benefits, and any questions around antipsychotic prescriptions. Sometimes both providers and patients and families can be helped through shared decision-making. We hope that robust patient decision aids will be developed to assist conversations around pediatric antipsychotic use.
  - Clearly identify target symptoms for which the antipsychotic medication is being prescribed.
  - Follow the American Academy of Child and Adolescent Psychiatry practice parameter for the use of atypical antipsychotic medications in children and adolescents
  - If antipsychotics have been prescribed, continue to offer psychosocial interventions.
  - Revisit need for antipsychotics every six months.
- Monitoring Effectiveness and Side Effects
  - Talk to the child and parent or guardian about possible side effects and provide guidance on how to identify side effects such as movement disorders.

    - Measure baseline weight, height, blood glucose, cholesterol, and triglyceride levels prior to starting medication.
    - Measure again at 4 weeks, 8 weeks, 12 weeks and then every 3 months for one year, every 6 months after the first year. Additional visits may be necessary.
    - Regularly reassess the effect of medication on symptoms, side effects and the need for ongoing medication, every 6-12 months, with the child, parents, and caregivers.
- Supporting parents in interacting with schools
    - Review Office of the Superintendent of Public Instruction resources on special education www.k12.wa.us/SpecialEd/Families/default.aspx.
    - Provide a documented diagnosis to support the patient's Individual Education Plan.

### Behavioral Health Care Providers (Prescribers and Non-Prescribers)

- Coordinate care with the prescribing clinician, especially reporting side effects or changes observed as well as beneficial impact on functioning, and schedule for reevaluating the need for antipsychotic medication.
- Provide increased level of psychosocial interventions and treatment in hopes of minimizing the need or shortening the duration of treatment with antipsychotic medication.
- Use evidence-based psychosocial interventions appropriate for the diagnoses. The following are components of evidence-based interventions:
    - Praise
    - Time out
    - Tangible rewards
    - Commands (coaching to deliver clear and uncomplicated requests)
    - Problem solving
    - Differential reinforcement (pick your battles, extra praise on what you want to have happen)
    - Modeling
    - Cognitive (coaching different ways to think about things)
    - Psychoeducation for parents and caregivers
    - Monitoring
    - Communication skills
- Patients' initial status and their progress during treatment should be evaluated using a Diagnostic and Statistical Manual of Mental Disorders (DSM) validated behavior checklist (e.g., Vanderbilt Assessment Scale) to help assess possible causes of disruptive behavior or other behavioral health condition(s) and for possible comorbidities and other problems.

### Commercial and Medicaid Managed Health Plans

- Facilitate second opinion programs such as the Partnership Access Line. Promote development of financially viable models to support such programs.
- Provide coverage for mental health consultation services to be available for pediatricians and primary care physicians.
- Ensure adequacy of behavioral health network to provide comprehensive psychosocial evaluations and ongoing interventions.
- Provide coverage for tele-psychiatry when local resources are insufficient.
- Improve access and ease of referrals by clearly identifying and communicating the clinical scope of behavioral health providers.
- Adopt the 2015 HEDIS definitions around pediatric antipsychotic use and use them for quality improvement. See page 25. These include:
    - ***Metabolic monitoring for children and adolescents on antipsychotics:*** percentage of children and adolescents 1 to 17 years of age who had two or more antipsychotic prescriptions and had metabolic testing. (NQMC:010541)
    - ***Use of first-line psychosocial care for children and adolescents on antipsychotics****:* percentage of children and adolescents 1 to 17 years of age who had a new prescription for an antipsychotic medication and had documentation of psychosocial care as first-line treatment. (NQMC:010579)
    - ***Use of multiple concurrent antipsychotics in children and adolescents***: percentage of children and adolescents 1 to 17 years of age who were on two or more concurrent antipsychotic medications. (NQMC:010549)

### Washington State Health Care Authority

- Create a web-based system for prior authorization (modeled on Michigan's use of Magellan's "Pharmacy Web PA") that physicians and the Partnership Access Line can use to obtain prior authorization at the point of care rather than having parents/guardians be denied prescriptions at the pharmacy. https://webpa.fhsc.com/my.policy
- Consider your role in population surveillance.

### Behavioral Health Organizations

- Provide evidence-based treatment in line with the recommendations to behavioral health care providers.
- Document behavioral health diagnoses.
- Provide training to primary care providers and midlevel providers (e.g., nurse practitioners, physician assistants)

## Background

Estimates of the prevalence of any mental disorder in children between the ages of 13-18 years is 46.3%, 21.4% having a severe disorder within that time period. [8] Among 8-15 year olds, 12 month prevalence of any disorder is 13.1%, including but not limited to 8.6% ADHD; 3.7% mood disorder, 2.7% major depression; 2.1% conduct disorder; 1% dysthymia; 0.7% anxiety disorder; 0.4% panic disorder). [9] Nationally, approximately 11% of children 4-17 years old are diagnosed with ADHD, 6.1% of whom take medication.[7] The prevalence of developmental disorders, including autism, is more common, at 16.7%.[10] Autism occurs in approximately 14.6 per 1,000 children (1.46%).[11]

Disruptive behaviors in children and adolescents are common. While many disruptive behaviors are developmentally appropriate, some persistent and severe behaviors may be associated with a diagnosis of ADHD, oppositional defiant disorder, or conduct disorder. Such behaviors can be disturbing to parents, caregivers, and family members, sometimes posing safety risks to family members and the child, and interrupting social and academic engagement and psychosocial development.

Off-label use of antipsychotics for the treatment of aggressive, impulsive, and disruptive behaviors, in the absence of psychosis[3] has become common practice due to a combination of factors, including:

- The ability of antipsychotic agents to dampen disruptive symptoms (even in the absence of psychosis) in many cases making it easier to provide care for the youth and making it possible for the youth to remain in school, in home, and receptive to other forms of therapy.
- The lower incidence of tardive dyskinesia with second-generation antipsychotics compared to first generation antipsychotics.[4]
- The lack of accessible and cost-effective behavioral therapy options—which are evidence-based first line treatments for disruptive disorders—especially outside of urban areas

The Food and Drug Administration (FDA) has approved five atypical antipsychotics for use in children and adolescents over five years old, aripiprazole, olanzapine, paliperidone, quetiapine, and risperidone for schizophrenia, bipolar I disorder: manic or mixed, and irritability with autistic disorder, see **Table 2**, on the following page. [12]

Antipsychotic use is increasing for patients under 21 years of age. Nationally, between 2002 and 2007, there was a 62% increase in antipsychotic use among children enrolled in Medicaid.[2] Additionally, in children two to five years old, antipsychotic use has increased from 0.78 to 1.59 per 1,000 children among privately insured children.[13] In this population, only 40.8% received a mental health assessment.[12] Among foster care children, recent research shows an increase (to two thirds) in provision of a psychosocial mental health intervention and in appropriate metabolic monitoring but that fewer than one third of other Medicaid insured children received a psychosocial intervention, showing the impact of increased oversight and need for spread.[4]

**Table 2: FDA-Approved Atypical Antipsychotics in Children and Adolescents**[14,15]

| Generic Name | Indications | Age Group for Which Approved |
|---|---|---|
| **Aripiprazole** | Schizophrenia | 13–17 years |
| | Bipolar disorder (manic/mixed) monotherapy or adjunctive to lithium or valproate | 10–17 years |
| | Irritability with autistic disorder | 6–17 years |
| **Olanzapine** | Schizophrenia<br>Bipolar disorder (manic/mixed) | 13–17 years |
| **Paliperidone** | Schizophrenia | 12–17 years |
| **Quetiapine** | Schizophrenia | 13–17 years |
| | Bipolar disorder (acute manic) | 10–17 years |
| **Risperidone** | Schizophrenia | 13–17 years |
| | Bipolar disorder (manic/mixed) | 10–17 years |
| | Irritability with autistic disorder | 5–16 years |

## Pediatric Antipsychotic Use in Washington State

Within the 2011 Washington State Medicaid fee-for-service program 6.4% of enrolled children (under 18 years) were prescribed a mental health drug and 1.1% were prescribed antipsychotics.[16] Antipsychotics were prescribed for 0.1% of children ≤5 years old and 6.2% of foster care children.[16] Across thirteen integrated delivery systems in the United States who are part of the mental health research network, rates of antipsychotic use vary by diagnosis and age group.

**Table 3: Rates of Antipsychotic Use by Age and Diagnosis**[i]

| Youth aged 0-17 with a diagnosis of: | 0-5 years | 6-11 years | 12-17 years |
|---|---|---|---|
| **Attention disorder** | 5% | 6% | 8% |
| **Autism spectrum disorder** | 2.7% | 15% | 27% |
| **Disruptive behavior diagnosis** | 4% | 11.9% | 16.7%. |

However these diagnoses were not necessarily the only mental health diagnoses these children received (e.g., antipsychotics may have been prescribed to a child with both an autism spectrum disorder and ADHD diagnosis).

[i] Data provided by Penfold, R from the Mental Health Research Network. September 2016.

### Antipsychotic Benefits

While there are many studies reporting on the beneficial and harmful side effects of atypical antipsychotics for adults, pediatric-specific literature especially is much less robust. Additionally, studies rarely include information on whether patients are also participating in psychosocial interventions or include any information on long-term effects of antipsychotic medication. However, clinically and anecdotally, antipsychotics have consistently shown to reduce aggressive, impulsive, and disruptive behaviors and there have been several published literature and comparative effectiveness on antipsychotic use in pediatrics.

The Agency for Health Care Research and Quality (AHRQ) has recently released a 2016 draft comparative effectiveness review, revising the 2012 version, of First- and Second-Generation Antipsychotics for Children and Young Adults. The 2016 re-review found thirteen studies examining ADHD, disruptive, impulse-control, or conduct disorders, an increase from eight studies in 2012.[17,18] The 2016 AHRQ re-review concluded that atypical antipsychotics, and risperidone alone, **probably** reduces conduct problems and aggression in children with ADHD who have not responded to stimulant medications and reduce severity more for patients with a primary diagnosis of disruptive, impulse-control, or conduct disorder.

Two large studies of risperidone found aggressive behaviors to be controlled in three to four weeks (using 1.5 mg/day), effective for subsequent six months controlled to group given a placebo.[16] A double-blind study of risperidone in children with autism found a 69% response rate in the control group.[16]

The Cochrane review, mentioned above, found eight randomized controlled trials assessing efficacy (seven risperidone, one quetiapine) in disruptive disorders (e.g., reduction in aggression, reduction in conduct problems or disruptive behavior problems).[17] Reviewers found a range of effect sizes in the trials and conducted meta-analysis of aggression and conduct problems using the Aberrant Behavior Checklist Irritability subscale (used in three studies) finding a statistically significant reduction, the Overt Aggression Scale (used in two studies) finding non-significant results, the Nisonger Child Behaviour Rating Form – Conduct Problem subscale (used in two studies) finding a significant reduction, and the Conners' Parent Rating Scale – Conduct Problem subscale which found no effect. However, the studies did not include information on whether patients were also participating in psychosocial interventions and no studies included long-term effects of antipsychotic medication.

### Antipsychotic Side-Effects or Harms

Although atypical antipsychotics may be perceived as being safer than first generation agents, increasing evidence shows that use is associated with patient harms including obesity, cardiovascular effects including hypertension, the possibility of tics, and other effects on the developing brain.[5] Long- term research on the effects of atypical antipsychotic use in youth is lacking. There is a gap in the evidence especially with regards to the long-term effects of antipsychotic use in those under 21 years old.

**Table 4: Evidence for Harms from Antipsychotics**[7,14-20]

| | Specific Harm | Strength of Evidence |
|---|---|---|
| **Rare but serious allergic reaction** | | |
| **Metabolic/Endocrine** | Weight gain | Most common side effect |
| | Impaired glucose metabolism | Low-strength compared to placebo[15] |
| | Dyslipidemia | Low-strength compared to placebo[15] |
| | Elevated prolactin | Moderate-strength compared to placebo[15] |
| **Neurological** | Headache | Some evidence |
| | Sedation/Drowsiness | Moderate-strength compared to placebo[15] |
| | Tardive dyskinesia | Not supported by the literature, but anecdotal evidence |
| **Cardiovascular** | Hypertension | From multiple studies[20] |
| | Sudden cardiac death | Evidence from studies in adults |
| | Low blood pressure | Some evidence |

Studies commonly find that weight gain may be greater in children than in adults that antipsychotics are associated with diabetes, and that diabetes as a side effect may be independent from a patient's weight gain.[19] The 2012 review found weight gain/body composition, dyslipidemia (abnormally elevated blood cholesterol or fats), elevated prolactin (the hormone related to milk production), insulin resistance, and sedation to be significant side effects of atypical antipsychotics, the effects of which differed between specific drugs.[16] The strength of evidence for all side effects ranged from low to moderate.

Other reviews have found similar side-effects. The most common side-effects appear to be weight gain, headache, and drowsiness.[20] Studies have found no significant influence on overall growth or sexual maturity.[16] A Cochrane review of atypical antipsychotics for disruptive behavior disorders in patients 5 to 18 years of age found only two studies that included weight gain as an outcome, meta-analysis found an average of 5.2 pounds gained when compared to placebo.[21] Other side effects included headaches, dizziness, fatigue, neurological (e.g., agitation, muscle stiffness), gastrointestinal (e.g., vomiting, nausea). Other studies have found significant weight gain and metabolic effects. A 2015 AHRQ review of Psychosocial and Pharmacologic Interventions for Disruptive Behavior in Children and Adolescents found the largest risperidone study to report weight gain occurring in 1.2-6.5% of children, somnolence occurring in 1.7-11.6% of children, and that 35% of patients experienced an adverse event.[22] Weight gain appears to be highest with clozapine and olanzapine, but both risperidone and quetiapine have been associated with weight gain as well.[14]

Although outside of this report's population of interest, a study of second generation antipsychotics for children and adolescents with early-onset schizophrenia and schizoaffective disorder found weight gain in those treated with olanzapine of 13.4lbs as well as increases in total cholesterol, low density lipoprotein cholesterol, insulin, alanine aminotransferase, and aspartate aminotransferase levels.[23] In the study, patients prescribed risperidone gained an average of 8lbs and those prescribed molindone, a

first generation antipsychotic, gained no weight on average. Cardiovascular harms, including sudden cardiac death, have also been seen in both pediatric and adult patients when using antipsychotics due in part to increased blood pressure.[24]

## Schools

There is much variation between how schools identify children in need and in access to educational and appropriate developmental resources. In some cases, identification of problematic behaviors in the school setting can cause school staff to recommend use of antipsychotics, contributing to inappropriate use. Section 504 of the Federal Rehabilitation Act of 1973 is "*designed to protect the rights of individuals with disabilities in programs and activities that receive Federal financial assistance from the U.S. Department of Education (ED) [saying] 'No otherwise qualified individual with a disability in the United States . . . shall, solely by reason of her or his disability, be excluded from the participation in, be denied the benefits of, or be subjected to discrimination under any program or activity receiving Federal financial assistance*'."[25]

A 504 Individual Accommodation Plan identifies a student's disability and allows access to the school's regular educational services. The Individuals with Disabilities Education Act (IDEA) "*governs how states and public agencies provide early intervention, special education and related services to more than 6.5 million eligible infants, toddlers, children and youth with disabilities*."[26] IDEA mandates that school districts identify and evaluate children with disabilities, regardless of severity, up to age 21 as part of "Child Find."[26] An Individualized Education Plan (IEP) is then designed around individual students and guide "teachers, parents, school administrators, related services personnel, and students (when appropriate)" to improve educational results for children with disabilities.[27] Review: http://www.k12.wa.us/SpecialEd/Families/HowItWorks.aspx

- Special education: www.k12.wa.us/specialed/
- Section 504 worksheet: www.k12.wa.us/SpecialEd/present/2014/504_Handout_WASA_2014.pdf

**Table 5: Special Education Steps under IDEA**[26]

1. Child is identified as possibly needing special education and related services.
2. Child is evaluated.
3. Eligibility is decided.
4. Child is found eligible for services.
5. IEP meeting is scheduled.
6. IEP meeting is held and the IEP is written.
7. Services are provided.
8. Progress is measured and reported to parents.
9. IEP is reviewed.
10. Child is reevaluated (at least every three years).

Additional resources are also available including:

- Dispute resolution: www.k12.wa.us/SpecialEd/DisputeResolution/default.aspx
- Special Education Resource Library: www.k12.wa.us/SpecialEd/ResourceLibrary/default.aspx
- The National Center on Disability and Access to Education: www.ncdae.org/
- Guide to Assessment in Early Childhood: Infancy to Age Eight: www.k12.wa.us/EarlyLearning/GuideAssess.aspx
- Partnerships for Action. Voices for Empowerment: http://wapave.org/programs/parent-training-and-information/advocacy-education-links/
- Disabilities, Opportunities, Internetworking, and Technology Washington State Resources for Parents of Children and Youth with Disabilities: www.washington.edu/doit/washington-state-resources-parents-children-and-youth-disabilities
- Wright's Law Special Education Advocacy: www.wrightslaw.com/info/advo.index.htm

## Initial Evaluation

All children should be evaluated within the context of their whole family dynamic. During evaluation, clinicians should consider learning disabilities or developmental problems as well as an autism spectrum diagnoses. For patients with ADHD, stimulant medications should be tried and dose optimized as necessary prior to antipsychotics.

Patients should be evaluated using a Diagnostic and Statistical Manual of Mental Disorders (DSM) validated behavior checklist (e.g., Vanderbilt Assessment Scale) to help assess possible causes of disruptive behavior or other behavioral health condition(s) and for possible comorbidities and other problems. The University of Washington has a high-quality resource library of screening and surveillance tools for child and adolescent mental health available here: https://depts.washington.edu/dbpeds/Screening%20Tools/ScreeningTools.html.

Possible instruments include:

- Aberrant Behavior Checklist Irritability subscale
- Behavioral Assessment Program (BAS)
- Child Behavior Checklist Externalizing Problems
- Conners' Parent Rating Scale
- Eyberg Child Behavior Inventory
- Nisonger Child Behaviour Rating Form – Conduct Problem subscale
- Overt Aggression Scale
- Pediatric Symptom Checklist
- Vanderbilt Assessment Scale

## Psychosocial Interventions and Access

Meta analyses of psychosocial interventions have found that active parental involvement consistently contributes to significantly lower disruptive or aggressive behavior, benefiting patients and families.[20] Effective factors that are common to successful supportive psychosocial interventions, in decreasing order of how frequently they are used, include:[28]

1. Praise
2. Time out
3. Tangible rewards
4. Commands (i.e., coaching to deliver clear and uncomplicated requests)
5. Problem solving
6. Differential reinforcement (e.g., pick your battles, extra praise on what you want to have happen)
7. Modeling
8. Cognitive (i.e., coaching different ways to think about things)
9. Psychoeducation for the parent(s)
10. Monitoring
11. Communication skills

This often takes the form of retraining parental and child interaction. However, psychosocial interventions for disruptive, aggressive, or impulsive disorders for which antipsychotics are not an FDA-approved treatment but are commonly used, can vary significantly both in terms of quality and technique. There have been no harms from psychosocial interventions reported in the literature.[20]

Functional analysis "identification of variables that influence the occurrence of problem behavior" is included in many structured psychosocial interventions.[29] The 2015 AHRQ review of psychosocial and pharmacological interventions found 66 studies that addressed the effectiveness of psychosocial interventions, separating findings by patient age (preschool, school age, teenage).[20] Interventions for preschool children (N=23) mainly assessed Incredible Years, Parent-Child Interaction Therapy, or Triple P and all included the parent in the intervention. About half of all (N=29) the interventions for school-age children evaluated a more common, standardized intervention as was done for preschool children (e.g., Parent Management Training Oregon, Coping Power Program, Stop Now, SNAP Under 12). Interventions for teenage children (N=14) focused on Multisystemic Therapy, Brief Strategic Family Therapy, or other multi-component intervention. Although results were inconsistent and the studies used different outcome measures, multicomponent interventions (including both parent, child, and in some instances others such as teacher) or those that included the parent or caregiver found more success than interventions including only the patient or the control groups.[15]

By large, psychosocial interventions were more effective than no intervention at reducing unwanted behaviors. Targeting parent practices by increasing in-home predictability, consistency, and follow-through and effective discipline coupled with positive feedback for appropriate behaviors and ignoring negative behaviors are also successful techniques.[30] This is especially true for children under the age of eight. Unfortunately there are no studies looking at the relative effectiveness of psychosocial

interventions compared with antipsychotic or other pharmacologic interventions.[20] Given the available research, it is not possible to say that any one psychosocial intervention is more effective than any other, but that active parental involvement and multimodal components are more strongly associated with a greater reduction in symptoms.

Availability of these interventions is variable around the state. Barriers include lack of providers, scheduling issues, reimbursement.

### Behavioral Health Integration

Behavioral health has traditionally been siloed from physical health care. There is far greater stigma attached to mental health and substance abuse diagnoses than for other conditions; a less developed infrastructure for measuring and improving care quality; the need for connecting a greater variety and number of clinicians, specialists, and organizations; lower use of health information technology; and barriers in the health insurance marketplace.[31] Behavioral health integration has been shown to increase access to behavioral health services through decreased reliance on and better access to appropriate and appropriately timed specialty care and to be more patient-centered, cost-saving, and result in healthier patients and healthier populations.[32]

Behavioral Health Organizations (BHOs) are part of Washington State's efforts to build a Healthier Washington through the integration of behavioral and physical health. Senate Bill 6312, passed in 2014, directed the Department of Social and Health Services to "integrate funding and oversight for behavioral health (mental health and substance use) treatment services…to better coordinate care for people with co-occurring disorders."[33] The effect of this was to move from state-purchased behavioral health through the previous Regional Support Networks and counties to "Behavioral Health Organizations (BHOs) to purchase and administer public mental health and substance use disorder services under managed care."[34] BHOs are responsible for delivering short-term mental health treatment in the clinic and through Apple Health and managing services for patients who need services not covered by Apple Health and substance abuse services. More information on patient benefits can be found here: https://www.dshs.wa.gov/sites/default/files/BHSIA/dbh/BHO/Benefits_Book_English.pdf

Integrated funding is the first step to integrating behavioral health services into primary care for adults and children. A Bree Collaborative Behavioral Health Integration workgroup is currently developing minimum standards for integrating behavioral health into primary care including how to overcome barriers such as access to shared electronic health records, utilizing telehealth when necessary and appropriately, and working with 42 CFR. Workgroup materials and the final recommendation will be available here: www.breecollaborative.org/topic-areas/behavioral-health/

Ideally, pediatric patients would be able to receive evidence-based behavioral health care within their primary care clinic that is tailored to meet their needs. This would include access to psychiatric consultation both for the primary care staff and for the patient and family, either in-person or through telehealth. The patient's health would be supported by a shared care plan that is accessible to all members of the integrated care team and the care team would support the patient and family to build a culture of patient and family resilience and self-care strategies.

## Prescribing Practice

A 2013 review of 11 existing clinical practice guidelines for antipsychotic use in children measured whether the guidelines addressed seven quality domains known for relevance to best-practice clinical prescribing and management including whether the guidelines addressed use in patients with no primary indication, the population of interest for this Report and Recommendation.[35] Seven of the guidelines addressed use of antipsychotics with no clinical indication, described below. The other factors addressed by the review include: how to use for very young children, multiple concurrent antipsychotics, dose limits, access to psychosocial interventions, metabolic monitoring, and follow-up prescriber visits.

Three of the guidelines are from the American Academy of Child and Adolescent Psychiatry: focused on oppositional defiant disorder published in 2007, [36] on very young children published in 2007 as well, [37] and on atypical antipsychotic medications in children and adolescents published in 2011.[14] The American Academy of Child and Adolescent Psychiatry *practice parameter for the use of atypical antipsychotic medications in children and adolescents* lists 19 guidelines in the prescribing of antipsychotics for children and adolescents including:

1. Prior to the initiation of and during treatment with an atypical antipsychotic agent (AAA), the general guidelines that pertain to the prescription of psychotropic medications should be followed
2. When selecting any AAA for use in a child or adolescent, the clinician should follow the most current available evidence in the scientific literature
3. Due to the specific risks associated with the use of AAAs, additional factors to address, prior to the initiation of treatment with the AAAs, include obtaining a personal and family history of diabetes and hyperlipidemia, seizures and cardiac abnormalities, as well as any family history of previous response or adverse events associated with AAAs
4. Dosing of the AAAs should follow the "start low and go slow" approach and seek to find the lowest effective dose, recognizing that dosing may differ based on the targeted symptoms and patient diagnosis
5. Target dosing should be supported by the current literature and will vary depending on the condition being treated
6. If side effects do occur, a trial at a lower dose should be considered; however, certain side effects may preclude further treatment with the specific AAA
7. The use of multiple psychotropic medications in refractory patients may, at times, be necessary but has not been studied rigorously and clinicians should proceed with caution
8. The simultaneous use of multiple AAAs has not been studied rigorously and generally should be avoided
9. After the failure of one AAA the selection of an alternative medication may include consideration of another AAA and/or a medication from a different class of drugs

10. The acute and long-term safety of these medications in children and adolescents has not been fully evaluated and therefore careful and frequent monitoring of side effects should be performed
11. BMI should be obtained at baseline and monitored at regular intervals throughout treatment with an AAA
12. Careful attention should be given to the increased risk of developing diabetes with the use of AAA, and blood glucose levels and other parameters should be obtained at baseline and monitored at regular intervals
13. In those patients with significant weight changes and/or a family history indicating high risk, lipid profiles should be obtained at baseline and monitored at regular intervals
14. Measurements of movement disorders utilizing structured measures, such as the Abnormal Involuntary Movement Scale, should be done at baseline and at regular intervals during treatment and during tapering of the AAA
15. Due to limited data surrounding the impact of AAAs on the cardiovascular system, regular monitoring of heart rate, blood pressure and EKG changes should be performed
16. Although there is a relationship between AAA use and elevations of prolactin, the current state of evidence does not support the need for routine monitoring of prolactin levels in asymptomatic youths
17. Due to drug-specific risks, additional monitoring should be considered for specific AAAs
18. The limited long-term safety and efficacy data warrants careful consideration, before the initiation of medication, of the planned duration of the medication trial
19. Abrupt discontinuation of a medication is not recommended

Additionally, Choosing Wisely, a national initiative working toward increasing conversations about wasteful health care, the American Psychiatric Association recommends against pediatric antipsychotic overuse saying: [38]

- "*Don't routinely prescribe antipsychotic medications as a first-line intervention for children and adolescents for any diagnosis other than psychotic disorders [and]*
- *Don't prescribe antipsychotic medications to patients for any indication without appropriate initial evaluation and appropriate ongoing monitoring."*

Canadian guidelines on pharmacotherapy for disruptive and aggressive behavior in children and adolescents with attention-deficit hyperactivity disorder, oppositional defiant disorder, or conduct disorder were published after the review in 2015.[39] These guidelines recommend specific diagnosis and doses for specific antipsychotic drugs rather than clinical care pathways.

## Shared-Decision Making

Discussing the harms and benefits of antipsychotic use with both the child and family or caregiver when deciding to prescribe to children is critical.[40] For adults, literature on use of shared decision making for antipsychotic prescription is mixed, mainly due to patients being seen as lacking capacity to engage in shared decision making.[41] Type of antipsychotic medication does fit criteria for preference-sensitive care and shared decision making is believed to improve outcomes.

The Pediatric Antipsychotic Use workgroup reviewed AHRQ's Antipsychotic Medicines for Children and Teens: A Review of the Research for Parents and Caregivers. The guide is available here: http://www.ncbi.nlm.nih.gov/books/NBK109556/pdf/Bookshelf_NBK109556.pdf. This AHRQ guide was developed using the 2011 AHRQ review of off-label use of atypical antipsychotics that is currently being updated. We anticipate an updated patient decision aid will be made available following completion of the review. Our workgroup believes this guide is a good conversation starter, especially in listing questions for parents and caregivers to ask their providers about antipsychotic use. We list some of these questions for parents on page 7 and 8 of this Report and Recommendation. However, we believe that the guide many be confusing or overly burdensome.

The Ottawa Hospital research institute, which rates patient decision aids across International Patient Decision Aid Standards, also reviewed AHRQ's guide across content criteria (e.g., whether the aid describes the condition (health or other) related to the decision), development process criteria (e.g., whether field testing showed that people who were undecided felt that the information was presented in a balanced way), and effectiveness criteria (e.g., whether there is evidence that the decision aid (or one based on the same template) helps people know about the available options and their features) here: https://decisionaid.ohri.ca/Azsumm.php?ID=1524. The group rated this guide 8/11; 3/9; and 0/2 on these three areas respectively showing significant gaps.

The workgroup would like to see additional work to develop a comprehensive patient decision aid for pediatric antipsychotic prescribing.

## Vulnerable Populations

### Foster Children

Foster children have historically been prescribed antipsychotics at rates much higher than the general population due to early life experiences and disruption in parenting continuity. In Washington State this was six times the rate of other children receiving care through Medicaid.[16] Recent research has shown the rate of growth to have tapered off after 2008 but rates of use still remain high.[4]

Senate Bill 1879 that took effect July 24, 2015 directs the Health Care Authority to "*require a second opinion review from an expert in psychiatry for all prescriptions of one or more antipsychotic medications of all children under eighteen years of age in the foster care system. Thirty days of a prescription medication may be dispensed pending the second opinion review. The second opinion feedback must include discussion of the psychosocial interventions that have been or will be offered to the child and caretaker if appropriate in order to address the behavioral issues brought to the attention of the prescribing physician*."[42]

## Monitoring Effectiveness and Side Effects

Providers should monitor the impact of the antipsychotic medication on the disruptive behavior. We recommend that primary care providers measure baseline weight, height, blood glucose, cholesterol, and triglyceride levels prior to starting medication and also talk to the parent or guardian about side effects and how to identify side effects such as movement disorders. The above should again be measured at four weeks, eight weeks, 12 weeks and then every three months for one year, every six months after the first year and the effect of medication on symptoms and side effects should also be regularly assessed at least every six-12 months.

In the 2013 review of 11 clinical practice guidelines for antipsychotic use in children, eight recommend metabolic monitoring.[20] The American Academy of Child and Adolescent Psychiatry endorse the American Diabetes Association and American Psychiatric Association recommendations that measurements be taken prior to or immediately after an antipsychotic prescription including:[43]

- Personal and family history of obesity diabetes, dyslipidemia, hypertension, or cardiovascular disease
- Weight and height (so that BMI can be calculated)
    - Weight reassessed 4, 8, and 12 weeks after initiating or changing SGA therapy and quarterly thereafter at the time of routine visits
- Blood pressure
    - Reassessed three months post-drug initiation
- Fasting plasma glucose
    - Reassessed three months post-drug initiation
- Fasting lipid profile
    - Reassessed three months post-drug initiation

## Measurement

We encourage health plans to use the recent Healthcare Effectiveness Data and Information Set (HEDIS) measures introduced in 2015 for antipsychotic use in children and adolescents. These measures include:[44]

**Metabolic monitoring for children and adolescents on antipsychotics: percentage of children and adolescents 1 to 17 years of age who had two or more antipsychotic prescriptions and had metabolic testing.**

*Numerator:* Both of the following during the measurement year (1) at least one test for blood glucose or hemoglobin A1c (HbA1c) and (2) at least one test for low-density lipoprotein-cholesterol (LDL-C) or cholesterol

*Denominator:* Children and adolescents age 1 to 17 years as of December 31 of the measurement year with at least two antipsychotic medication dispensing events of the same or different medications on different dates of service during the measurement year

More information: www.qualitymeasures.ahrq.gov/summaries/summary/49739/metabolic-monitoring-for-children-and-adolescents-on-antipsychotics-percentage-of-children-and-adolescents-1-to-17-years-of-age-who-had-two-or-more-antipsychotic-prescriptions-and-had-metabolic-testing

**Use of multiple concurrent antipsychotics in children and adolescents: percentage of children and adolescents 1 to 17 years of age who were on two or more concurrent antipsychotic medications.**

*Numerator:* Members on two or more concurrent antipsychotic medications for at least 90 consecutive days during the measurement year

*Denominator:* Children and adolescents age 1 to 17 years as of December 31 of the measurement year with 90 days of continuous antipsychotic medication treatment during the measurement year

More information: www.qualitymeasures.ahrq.gov/summaries/summary/49749/use-of-multiple-concurrent-antipsychotics-in-children-and-adolescents-percentage-of-children-and-adolescents-1-to-17-years-of-age-who-were-on-two-or-more-concurrent-antipsychotic-medications#593

**Use of first-line psychosocial care for children and adolescents on antipsychotics: percentage of children and adolescents 1 to 17 years of age who had a new prescription for an antipsychotic medication and had documentation of psychosocial care as first-line treatment.**

*Numerator:* Documentation of psychosocial care in the 121-day period from 90 days prior to the Index Prescription Start Date (IPSD) through 30 days after the IPSD

*Denominator:* Children and adolescents age 1 to 17 years as of December 31 of the measurement year, with a Negative Medication History, who were dispensed an antipsychotic medication during the Intake Period

More information: www.qualitymeasures.ahrq.gov/summaries/summary/49782/use-of-firstline-psychosocial-care-for-children-and-adolescents-on-antipsychotics-percentage-of-children-and-adolescents-1-to-17-years-of-age-who-had-a-new-prescription-for-an-antipsychotic-medication-and-had-documentation-of-psychosocial-care-as-firstline-tre

## Implementation Considerations

Implementation of these recommendations is a key part of the Bree Collaborative's work. There are many barriers to aligning actual patient and family experience with the best practices discussed in this Report and Recommendations. Some issues include lack of:

- Primary care training on working with children and adolescents with aggressive, impulsive, and disruptive behaviors
- Primary care provider time to assess, interview, and develop interventions with and for children and families or caregivers
- Robust patient decision aids to support both providers and patient and families in shared decision making about antipsychotic prescribing harms and benefits
- Capacity and funding for second opinion services
- Behavioral health workforce and supporting infrastructure especially outside of urban areas
    - Washington State House Bill 2436 passed in 2016 formed a Children's Mental Health workgroup to review issues around "increasing access to adequate and appropriate mental health services for children and youth." A final report is expected in December 2016.
- Integration of behavioral health care into primary care
- Reimbursement for behavioral health care services

**Clinician Decision Support**

Literature for clinician decision support around antipsychotic prescribing especially in pediatrics is lacking. In adults an intervention to decrease antipsychotic polypharmacy in the New York State Office of Mental Health with a web-based clinical decision support tool followed by provider feedback was successful in reducing polypharmacy at six months to from 16.9 to 3.1 inpatients per 1,000.[45] Provider training is necessary to reduce inappropriate antipsychotic prescribing and is supported by tracking of provider antipsychotic prescribing to children under 21.[40]

Second opinion or consultation line programs have been studied in more detail and seem to be more widely used and successful. These programs are a voluntary or mandatory service providing primary care clinicians or others access to in-depth review of specific patient cases by a psychiatrist or other mental health professional. These programs have shown to be successful and cost-saving when applied to stimulant medications for ADHD in Washington State, resulting in savings of $1.2 million and 538 fewer patients exceeding pre-determined safety thresholds from May 2006 to April 2008.[46]

The Washington State Legislature prioritized high-quality children's mental health care in 2007 by expanding psychosocial services for children who get their care through Medicaid. Part of this included creating a program called the Partnership Access Line (PAL) to give primary care clinicians the opportunity to talk to experts about different types of medication used to treat behavioral health issues including antipsychotics. This is a "*telephone based child mental health consultation system for primary care providers funded by the Washington State legislature. PAL employs child psychiatrists and social workers affiliated with Seattle Children's Hospital to deliver its consultation services…[and] is available to primary care doctors, nurse practitioners and physician assistants throughout Washington State*."

## Appendix A: Bree Collaborative Members

| Member | Title | Organization |
|---|---|---|
| Susie Dade MS | Deputy Director | Washington Health Alliance |
| John Espinola MD, MPH | Executive Vice President, Health Care Services | Premera Blue Cross |
| Gary Franklin MD, MPH | Medical Director | Washington State Department of Labor and Industries |
| Stuart Freed MD | Chief Medical Officer | Confluence Health |
| Richard Goss MD | Medical Director | Harborview Medical Center – University of Washington |
| Christopher Kodama MD | President, MultiCare Connected Care | MultiCare Health System |
| Daniel Lessler MD, MHA | Chief Medical Officer | Washington State Health Care Authority |
| Paula Lozano MD, MPH | Associate Medical Director, Research and Translation | Group Health Cooperative |
| Wm. Richard Ludwig MD | Chief Medical Officer, Accountable Care Organization | Providence Health and Services |
| Greg Marchand | Director, Benefits & Policy and Strategy | The Boeing Company |
| Robert Mecklenburg MD | Medical Director, Center for Health Care Solutions | Virginia Mason Medical Center |
| Kimberly Moore MD | Associate Chief Medical Officer | Franciscan Health System |
| Carl Olden MD | Family Physician | Pacific Crest Family Medicine, Yakima |
| Mary Kay O'Neill MD, MBA | Partner | Mercer |
| John Robinson MD, SM | Chief Medical Officer | First Choice Health |
| Terry Rogers MD (Vice Chair) | Chief Executive Officer | Foundation for Health Care Quality |
| Jeanne Rupert DO, PhD | Medical Director, Community Health Services | Public Health – Seattle and King County |
| Kerry Schaefer | Strategic Planner for Employee Health | King County |
| Bruce Smith MD | Medical Director | Regence Blue Shield |
| Lani Spencer RN, MHA | Vice President, Health Care Management Services | Amerigroup |
| Hugh Straley MD (Chair) | Retired | Medical Director, Group Health Cooperative; President, Group Health Physicians |
| Carol Wagner RN, MBA | Senior Vice President for Patient Safety | The Washington State Hospital Association |
| Shawn West MD | Family Physician | Edmonds Family Medicine |

## Appendix B: Pediatric Psychotropic Use Charter and Roster

### Problem Statement

Among psychotropic medications prescribed to pediatric patients, antipsychotics have great potential for overuse. Antipsychotics are often prescribed for aggressive and impulsive behaviors, rather than psychosis.[2] Antipsychotic prescribing increased for adolescents and young adults in the past ten years. Use is associated with patient harms including obesity, cardiovascular effects including hypertension, the possibility of tics, and other effects on the developing brain.[3]

### Aim

To improve the appropriateness of antipsychotic drug prescribing to pediatric patients in the State of Washington supported by behavioral health services.

### Purpose

To propose recommendations to the full Bree Collaborative on adherence to appropriate antipsychotic drug prescribing for children and youth under at 21 years, by:

1. Clarifying the evidence-base for effectiveness and harms of pediatric antipsychotic use.
2. Recommending methods to increase evidence-based, best practice prescribing of pediatric antipsychotic drugs.
3. Recommending techniques to increase use of evidence-based prescription consultation services in the context of holistic behavioral health care.
4. Recommending methods of streamlining processes to increase best-practice prescribing to reduce waste and provider burden.
5. Identifying additional psychotropic prescribing areas for improvement.

### Duties & Functions

The Pediatric Psychotropic Use workgroup will:

- Research evidence-based guidelines and emerging best practices.
- Consult members of the Washington State Hospital Association, the Washington State Medical Association and other stakeholder organizations and subject matter experts for feedback, as appropriate.
- Meet for approximately nine months, as needed.
- Provide updates at Bree Collaborative meetings.
- Post draft report on the Bree Collaborative website for public comment prior to sending report to the Bree Collaborative for approval and adoption.
- Present findings and recommendations in a report.
- Recommend data-driven implementation strategies.
- Create and oversee subsequent subgroups to help carry out the work, as needed.

[2] Olfson M, King M, Schoenbaum M. Treatment of Young People With Antipsychotic Medications in the United States. JAMA Psychiatry. 2015 Sep;72(9):867-74.

[3] Agency for Healthcare Research and Quality. Antipsychotic Medicines for Children and Teens: A Review of the Research for Parents and Caregivers. US Department of Health and Human Services. September 4, 2012. Available: http://effectivehealthcare.ahrq.gov/index.cfm/search-for-guides-reviews-and-reports/?productid=1146&pageaction=displayproduct. Accessed: August 2015.

## Structure

The workgroup will consist of individuals appointed by the chair of the Bree Collaborative or the workgroup chair and confirmed by Bree Collaborative members.

The chair of the workgroup will be appointed by the chair of the Bree Collaborative.

The Bree Collaborative project director will staff and provide management and support services for the workgroup.

Less than the full workgroup may convene to: gather and discuss information; conduct research; analyze relevant issues and facts; or draft recommendations for the deliberation of the full workgroup. A quorum shall be a simple majority and shall be required to accept and approve recommendations to send to the Bree Collaborative.

## Meetings

The workgroup will hold meetings as necessary. The program director will conduct meetings along with the chair, arrange for the recording of each meeting, and distribute meeting agendas and other materials prior to each meeting. Additional workgroup members to be added at the discretion of the chair.

| Name | Title | Organization |
|---|---|---|
| Paula Lozano, MD, MPH (Chair) | Medical Director, Research and Translation | Group Health Cooperative |
| David Buchholz, MD | Medical Director, Provider Engagement | Premera Blue Cross |
| Shelley Dooley | Parent Advocate | |
| Nalini Gupta, MD | Pediatrician | Developmental and Behavioral Pediatrics, Providence Health and Services |
| Robert Hilt, MD | Director, Community Leadership; Director of Partnership Access Line | Seattle Children's |
| Liz Pechous, PhD | Clinical Director | ICARD, PLLC |
| Robert Penfold, PhD | Co-investigator, Mental Health Research Network | Group Health Research Institute |
| James Polo, MD, MBA | Chief Medical Officer | Western State Hospital |
| David Testerman, PharmD | Pharmacy Director | Amerigroup |
| Mark Stein, PhD | Director of ADHD and Related Disorders Program (PEARL Clinic) | Seattle Children’s |
| Donna Sullivan, PharmD, MS | Chief Pharmacy Officer | Washington Health Care Authority |

## Appendix C: Literature Review and Key Questions

We used a two-stage approach. First to search for key questions around antipsychotics and non-pharmacological treatment and second to search for key questions around influencing provider behavior.

**First Stage**

We searched MEDLINE® via PubMed® and the Cochrane Central Register of Controlled Trials. Search terms included "antipsychotic" plus harm or benefit or diagnosis by name (e.g., disruptive behavior, behavior disorder, or conduct disorder) plus non-pharmacological treatment by name (e.g., therapy or treatment or psychotherapy) and pediatric key words (e.g., pediatric, child, adolescent, teen, young adult). We limited our search to systematic reviews or meta-analyses published after 2006 (within the last ten years). Search exclusion criteria were studies focused on populations over 21 years of age, the population under review being diagnosed with on-label use of antipsychotics (e.g., schizophrenia), focused on first generation or typical antipsychotics, not in English, focused on prevention, or generally out of scope (e.g., psychopathology of hearing-impaired children).

Our population of interest is individuals under age 21 without a diagnosis of an FDA-approved indication for antipsychotic prescribing (e.g., schizophrenia, bipolar I disorder: manic or mixed, and irritability with autistic disorder).

**Key Questions**

**Antipsychotics**

1. What are the benefits of atypical antipsychotics in people age <21 y, by subgroup (age, diagnosis)
2. What are the harms of atypical antipsychotics in people age <21 y, by subgroup (age, diagnosis)

**Non-pharmacological treatment**

3. What are the benefits of non-pharmacological treatments for people age <21 y who have behavior problems (and may be considered candidates for antipsychotics*)?
   a. Behavior therapy, in person
   b. Behavior therapy, via telehealth
   c. Psychotherapy
4. What are the harms of non-pharmacological treatments for people age <21 y who have behavior problems (and may be considered candidates for antipsychotics*)?
   d. Behavior therapy, in person
   e. Behavior therapy, via telehealth
   f. Psychotherapy

**Results**

| Source | Met criteria | Area of focus | Included in draft report |
|---|---|---|---|
| MEDLINE (PubMed) | 28 | 16 on psychosocial interventions<br>13 on pharmacotherapy<br>1 both | 4 |
| Cochrane | 5 | 4 on psychosocial interventions = 4<br>1 on pharmacotherapy | 1 |
| Guidelines | 12 | 5 management of disruptive or aggressive disorders<br>5 on pharmacotherapy<br>2 general = 2 | 9 |

**Second Stage**

We searched MEDLINE® via PubMed® and the Cochrane Central Register of Controlled Trials. Search terms included "antipsychotic" or "antipsychotics" plus "decision support" and pediatric key words (e.g., pediatric, child, adolescent, teen, young adult). We limited our search to systematic reviews or meta-analyses published after 2006 (within the last ten years). Search exclusion criteria were studies focused on populations over 21 years of age, the population under review being diagnosed with on-label use of antipsychotics (e.g., schizophrenia), focused on first generation or typical antipsychotics, not in English, focused on prevention, or generally out of scope (e.g., psychopathology of hearing-impaired children).

**Influencing provider behavior**

5. What is the effectiveness of clinician decision support on influencing prescribing behavior regarding prescribing of antipsychotics in persons <21 y?

The search found 6 results but no results relevant to our key question and population of interest. Conducting the search without the pediatric key words found 68 results, two of which are relevant to the key question (although focused on adults and not restricted to our diagnostic categories).

## Appendix D: Summary of Guidelines

- **American Academy of Child and Adolescent Psychiatry. Practice parameter for the assessment and treatment of children and adolescents with oppositional defiant disorder. 2007.** Has 11 recommendations including:
    1. Successful treatment requires establishing a therapeutic alliance with both the family and the child.
    2. Actively consider cultural issues.
    3. Obtain information from both the child and the parents (e.g., core symptoms, age at onset, symptom duration, functional impairment degree).
    4. Consider comorbid conditions.
    5. Outside information may be helpful (e.g., from daycare, teachers, etc).
    6. Questionnaires and rating scales may be used to evaluate and track progress.
    7. Develop individualized treatment plan.
    8. Parent management training based on an empirically tested intervention is recommended that will "*reduce positive reinforcement of disruptive behavior; increase reinforcement of prosocial and compliant behavior; positive reinforcement varies widely, but parental attention is predominant; punishment usually consists of a form of time out, loss of tokens, and/or loss of privileges; Apply consequences and/or punishment for disruptive behavior; make parental response predictable, contingent, and immediate*."
    9. Medication should not be the sole intervention for oppositional defiant disorder saying, "*medications may be helpful as adjuncts to treatment packages, for symptomatic treatment and to treat comorbid conditions*" and that adherence, compliance, and diversion should be carefully monitored.
    10. Long-term treatment may be needed depending on severity.
    11. Short-term/one-time/time-limited and dramatic interventions are not effective.
- **Treatment of maladaptive aggression in youth: CERT guidelines II. Treatments and ongoing management. Scotto Rosato N, Correll CU, Pappadopulos E, et al. 2012.**[4] Created by the Center for Education and Research on Therapeutics (CERT) whose mission is to "*conduct research and provide education that will advance the optimal use of drugs, medical devices, and biological products; increase awareness of the benefits and risks of therapeutics; and improve quality while cutting the costs of care*."[5]
    1. *Initial Medication Treatment Should Target the Underlying Disorder (s) (Grade of Evidence: A; Strength of Recommendation: Very Strong)*
    2. *When Available, Follow Evidence Based Guidelines for the Primary Disorder (Grade of Evidence: A; Strength of Recommendation: Very Strong)*

[4] Scotto Rosato N, Correll CU, Pappadopulos E, et al. Treatment of maladaptive aggression in youth: CERT guidelines II. Treatments and ongoing management. Pediatrics. 2012;129:e1577–e1586.

[5] Agency for Healthcare Research and Quality. Centers for Education & Research on Therapeutics (CERTs). Accessed: May 2016. Available: http://certs.hhs.gov/index.html.

3. *Consider Adding an Antipsychotic Medication, Taking Into Account the Latest Available Evidence on Efficacy and Safety of Individual Agents, If Severe Aggression Persists After an Adequate Trial of Treatments for the Underlying Disorder (Including Psychosocial Treatments) (Grade of Evidence: A; Strength of Recommendation: Strong)*
4. *Use Recommended Titration Schedules and Deliver an Adequate Medication Trial Before Changing or Adding Medication (Grade of Evidence: A; Strength of Recommendation: Very Strong)*
5. *If Insufficient Response, Try a Different Antipsychotic Medication (Grade of Evidence: D; Strength of Recommendation: Strong)*
6. *For a Partial Response to an Initial First-Line Antipsychotic, Consider Augmentation With a Mood Stabilizer (Grade of Evidence: B; Strength of Recommendation: Strong)*
7. *Avoid Using More Than 2 Psychotropic Medications Simultaneously (Grade of Evidence: C; Strength of Recommendation: Very Strong)*

- **American Academy of Child and Adolescent Psychiatry. Psychopharmacological treatment for very young children: contexts and guidelines. 2007.** Gleason et al focus on recommendations for preschool aged children and developed treatment algorithms to guide psychopharmacological treatment of disorders. Assessment and diagnosis are the baseline for any intervention, structured baseline assessments being important to guide clinical care pathways and monitor response. Guidelines universal to all diagnoses include:
    1. "*Avoid medications when therapy is likely to produce good results*
    2. *Generally, an adequate trial of psychotherapy precedes consideration of medication, and psychotherapy continues if medications are used.*
    3. *Medications should be considered in the context of a clinical diagnosis and substantial functional impairment.*
    4. *A system should be developed to track symptoms and impairment before initiating treatment.*
    5. *Parent referral or treatment for psychopathology may optimize their ability to participate in treatment as well as family mental health.*
    6. *Informed consent includes explicit information about FDA approval and level of evidence supporting recommendations.*
    7. *The 'N of 1' trial approach should be considered when initiating medication treatment.*
    8. *Medication discontinuation trials are encouraged to reduce unnecessary medication treatment.*
    9. *The use of medications primarily to address side effects of other medications is not recommended*."
- **Treatment recommendations for the use of antipsychotics for aggressive youth (TRAAY). Pappadopulos E, Macintyre Ii JC, Crismon ML, et al. 2011. 2003.** [6] are meant to "provide a

[6] Pappadopulos E, Macintyre Ii JC, Crismon ML, et al. Treatment recommendations for the use of antipsychotics for aggressive youth (TRAAY). Part II. J Am Acad Child Adolesc Psychiatry. 2003;42:145–161.

systematic treatment guide for the management of aggressive symptoms in youth treated in structured psychiatric settings…developed with evidence, expert concensus, and survey data."

1. "Conduct an initial diagnosis evaluation before using pharmacological treatment.
2. Assess treatment effects and outcomes.
3. Begin with psychosocial and educational treatment.
4. Use appropriate treatment for primary disorders as a first time treatment.
5. Use an atypical antipsychotic first rather than a typical antipsychotic to treat aggression
6. Use a conservative dosing strategy (e.g., start low, go slow, taper slow). Atypical antipsychotic should be tried for a minimum of two weeks at an appropriate dose prior to being considered ineffective.
7. Use psychosocial crisis management techniques before medication for acute or emergency treatment of aggression.
8. Avoid frequent use of emergency (stat, p.r.n.) medications to control behavior.
9. Assess side effects routinely and systematically.
10. Ensure an adequate trial before changing medications."
11. Use a different atypical antipsychotic after a failure to respond to an adequate trial of the initial first line atypical
12. Consider adding a mood stabilizer after a partial response to an initial first-line antipsychotic
13. If a patient is not responding to multiple medications, consider tapering one or more medication(s)
14. Taper and consider discontinuing antipsychotics in patients who show remission in aggressive symptoms for six months or longer

- **Texas Department of Family and Protective Services and University of Texas at Austin College of Pharmacy. Psychotropic medication utilization parameters for foster children. 2013.**[7] This guideline was deemed out of scope for this Recommendation.

[7] Texas Department of Family and Protective Services and University of Texas at Austin College of Pharmacy. Psychotropic medication utilization parameters for foster children. Available at: www.dfps.state.tx.us/documents/Child_Protection/pdf/TxFosterCareParameters-September2013.pdf.

## Appendix E: Partnership Access Line Antipsychotics Fact Sheet Drug Utilization Review Program, Version 6.1, Summer 2015[47]

Washington State Health Care Authority

# Fact Sheet: Antipsychotics
# Drug Utilization Review Program

The following dosing guidelines regarding child antipsychotic medications were established by the Washington State Health Care Authority (HCA) Pediatric Advisory Group and Drug Utilization Review Board. Prescriptions outside of these dosing limits will require a safety/appropriate use review with a member of HCA's second opinion network.

*Child in crisis:* Families can receive an urgent medication fill of an antipsychotic prescription that will trigger a review per the below guidelines if they indicate at the pharmacy that their child is in crisis, or if the provider writes "child in crisis" on the prescription.

| Drug | Antipsychotic Dosing Limits* | | | |
|---|---|---|---|---|
| | Age under 3 | Age 3-5 years | Age 6-12 years | Age 13-17 years |
| Abilify® (aripiprazole) | Review required | Review required | 20 mg per day | 30 mg per day |
| Clozaril®/Fazaclo® (clozapine) | Review required | Review required | 600 mg per day | 900 mg per day |
| Geodon® (ziprasidone) | Review required | Review required | 80 mg per day | 160 mg per day |
| Haldol® (haloperidol) | Review required | Review required | 10 mg per day | 15 mg per day |
| Invega® (paliperidone) | Review required | Review required | Review required | Review required |
| Risperdal®/M-Tab® (risperidone) | Review required | 2 mg per day | 4 mg per day | 8 mg per day |
| Seroquel®/XR (quetiapine) | Review required | Review required | 300 mg per day | 600 mg per day |
| Trilafon® (perphenazine) | Review required | Review required | 12 mg per day | 24 mg per day |
| Zyprexa®/Zydis® (olanzapine) | Review required | 2.5 mg per day | 10 mg per day | 20 mg per day |

***Prescriptions exceeding dosing limitations for age require a HCA-approved second opinion**

**Antipsychotics for Children in Foster Care**

A state law (SHB 1879) taking effect 7/24/15 requires that a psychiatric expert provide a second opinion review of any use of an antipsychotic prescribed for more than 30 days to any child in foster care.

**Psychiatric Polypharmacy**

Other criteria under which HCA will initiate a required second opinion review of child psychiatric medications (as advised by the HCA Pediatric Advisory Group and Drug Utilization Review Board) include:

- Two (2) or more antipsychotic medications prescribed concomitantly after 60 days
- Five (5) or more different psychotropic medications prescribed concomitantly after 60 days

## Appendix F: Resources for Parents

**Canadian Alliance for Monitoring Effectiveness and Safety of Antipsychotics in Children** (CAMESA)
Guidelines for Parents available here: http://camesaguideline.org/information-for-parents

**Partnerships for Action Voices for Empowerment** (PAVE)
6316 South 12th Street
Tacoma, WA 98465-1900
Phone: (800) 572-7368 (Voice/TTY)
Fax: (253) 566-8052
e-mail: pave@wapave.org
website: www.wapave.org

**Special Education Advocacy.Org**
Organization focused on helping parents navigate IEP and 504 Plans
Phone: (888) 881-5904 / (206) 914-0975
www.specialeducationadvocacy.org

**Team Child**
Legal services for youth including outreach, trainings, and broader advocacy
1225 South Weller St, Suite 420 | Seattle, WA 98144
Phone: (206) 322-2444
Fax: (206) 381-1742
Email: questions@teamchild.org
www.teamchild.org/

**Treehouse: Giving Foster Kids a Childhood and a Future**
Resources to help parents ensure their child has access to education
2100 24th Avenue S. Suite 200 | Seattle, WA 98144-4643
Phone: (206) 767-7000
www.treehouseforkids.org/students/educational-advocacy/

**Washington Autism Alliance & Advocacy** (WAAA)
16225 NE 87th Street, Suite A-2
Redmond, WA 98052
Phone: (425) 836-6513
e-mail: info@WashingtonAutismAdvocacy.org
website: www.WashingtonAutismAdvocacy.org

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