Inclusion Criteria
- Children who are prescribed second-generation antipsychotic medications

Critically Analyze the Evidence

The GRADE criteria were used to evaluate the quality of evidence presented in research articles reviewed during the development of this guideline. The table below defines how the quality of evidence is rated and how a strong versus a weak recommendation is established.

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Type of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>STRONG</td>
<td>Desirable effects clearly outweigh undesirable effects or vice versa</td>
</tr>
<tr>
<td>WEAK</td>
<td>Desirable effects closely balanced with undesirable effects</td>
</tr>
<tr>
<td>Quality</td>
<td>Type of Evidence</td>
</tr>
<tr>
<td>High</td>
<td>Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies</td>
</tr>
<tr>
<td>Moderate</td>
<td>Evidence from RCTs with important limitations (e.g., inconsistent results, methodological flaws, indirect evidence, or imprecise results) or unusually strong evidence from unbiased observational studies</td>
</tr>
<tr>
<td>Low</td>
<td>Evidence for at least 1 critical outcome from observational studies, from RCTs with serious flaws or indirect evidence</td>
</tr>
<tr>
<td>Very Low</td>
<td>Evidence for at least 1 critical outcome from unsystematic clinical observations or very indirect evidence</td>
</tr>
</tbody>
</table>

PICO Question 1: Do children with mental health disorders (ages 3-17) who are prescribed second-generation antipsychotic medications (SGAs) have a decreased likelihood of adverse changes in weight, waist circumference, BMI, glucose intolerance, hypercholesterolemia, hypertriglyceridemia, and hyper-prolactin with scheduled monitoring of physical and laboratory measures vs. those children with mental health disorders who are prescribed SGAs and are not routinely monitored?

Recommendation: Strong recommendation with high quality evidence to routinely monitor physical and laboratory measures of the metabolic effects of SGAs. (1-11)

Currently there is limited pediatric data on the ability of routine physical and laboratory monitoring of the significant negative effects of SGAs on pediatric patients current and long term physical health. However, there is clear evidence that the SGAs, separate from the disorders they are being utilized for, can significantly increase central obesity, waist circumference, increase in IFG, DM2, increase triglycerides and LDL while lowering HDL, increase BP and prolactin (with risperidone primarily) in both adult and pediatric populations. Given that this class of medications are often used relatively long term (average 12+ months) and in combination with other agents also likely to worsen metabolic outcomes, routine monitoring in addition to specific recommendations for intervention, especially if from a psychiatric standpoint the medications are considered lifesaving, are absolutely necessary to address their current and long-term morbidity/mortality and quality of life.

The overall quality of the evidence is moderate; this stems from there not being much data in the pediatric population on these questions. The vast majority of the data is within the adult population. However, the expert consensus from the American Academy of Child and Adolescent Psychiatry, American Academy of Pediatrics, American Diabetes Association, and the American Psychiatric Association all indicate that routine monitoring is clinically indicated when a patient is taking a SGA, regardless of age.

Critical Points of Evidence*

- Routinely monitor physical and laboratory measures of the metabolic effects of SGAs. (1-11) – Strong recommendation, high quality evidence

*NOTE: The references cited represent the entire body of evidence reviewed to make each recommendation.
Apply the Evidence

- Develop protocols designed to assist physicians who prescribe this class of medications to pediatric patients for the necessary physical and laboratory monitoring required as well as highlight possible intervention strategies when certain physical or laboratory thresholds are crossed.
- As there is diversity in the type of psychiatric disorders being treated with this class of medications, there may be a tiered system of recommendations for monitoring and interventions dependent on the disorder and the functional impairment of the patient.
- We recommend first developing an all-inclusive process of clinician reminders which we could then utilize to develop research protocols to assess the best practices as it relates to pediatric mental health disorders and the patients who are prescribed this class of medications.
- We also recommend that all patients prescribed an SGA medication have the following elements monitored:
  - Baseline: Height, weight, waist circumference, body mass index, blood pressure, fasting glucose, lipid panel, prolactin, liver panel
  - 3, 6, 12 (annually) months post-initiation: Fasting glucose, lipid panel, prolactin, liver panel
  - Each clinical encounter: Height, Weight, Waist Circumference, Body Mass Index, Blood pressure

References

Clinical Standards Preparation
This clinical standard was prepared by the Evidence-Based Outcomes Center (EBOC) team in collaboration with content experts at Texas Children’s Hospital. Development of this clinical standard supports the TCH Quality and Patient Safety Program initiative to promote clinical standards and outcomes that build a culture of quality and safety within the organization.

EBP Course Participants and EBOC Support
Laurel L. Williams, DO
Diane Treadwell-Deering, MD
Kirti Saxena, MD
Christine Lobo, MPH, Research Specialist
Charles Macias, MD, MPH, Medical Director

Additional EBOC Support
Tom Burke, Research Assistant
Sherin Titus, Research Assistant

No relevant financial or intellectual conflicts to report.

Development Process
This clinical standard was developed using the process outlined in the EBOC Manual. The literature appraisal documents the following steps:

1. Review Preparation
   - PICO questions established
   - Evidence search confirmed with content experts
2. Review of Existing External Guidelines
   - N/A
3. Literature Review of Relevant Evidence
   - Searched: PubMed; Cochrane
4. Critically Analyze the Evidence
   - 4 nonrandomized studies, 1 systematic review, and 3 review articles
5. Summarize the Evidence
   - Materials used in the development of the clinical standard, literature appraisal, and any order sets are maintained in a Metabolic Monitoring of Second-Generation Antipsychotic Medications evidence-based review manual within EBOC.

Evaluating the Quality of the Evidence
Published clinical guidelines were evaluated for this review using the AGREE II criteria. The summary of these guidelines are included in the literature appraisal. AGREE II criteria evaluate Guideline Scope and Purpose, Stakeholder Involvement, Rigor of Development, Clarity and Presentation, Applicability, and Editorial Independence using a 4-point Likert scale. The higher the score, the more comprehensive the guideline.

This clinical standard specifically summarizes the evidence in support of or against specific interventions and identifies where evidence is lacking/inconclusive. The following categories describe how research findings provide support for treatment interventions.

“Evidence Supports” provides evidence to support an intervention “Evidence Against” provides evidence against an intervention.

Recommendation

<table>
<thead>
<tr>
<th>Quality</th>
<th>Type of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>STRONG</td>
<td>Desirable effects clearly outweigh undesirable effects</td>
</tr>
<tr>
<td>WEAK</td>
<td>Desirable effects closely balanced with undesirable effects</td>
</tr>
<tr>
<td>High</td>
<td>Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies</td>
</tr>
<tr>
<td>Moderate</td>
<td>Evidence from RCTs with important limitations (e.g., inconsistent results, methodological flaws, indirect evidence, or imprecise results) or unusually strong evidence from unbiased observational studies</td>
</tr>
<tr>
<td>Low</td>
<td>Evidence for at least 1 critical outcome from observational studies, RCTs with serious flaws or indirect evidence</td>
</tr>
<tr>
<td>Very Low</td>
<td>Evidence for at least 1 critical outcome from unsystematic clinical observations or very indirect evidence</td>
</tr>
</tbody>
</table>

Recommendations

Practice recommendations were directed by the existing evidence and consensus amongst the content experts. Patient and family preferences were included when possible. The Content Expert Team and EBOC team remain aware of the controversies in the metabolic monitoring of Second-Generation Antipsychotic Medications (SGAs) in children. When evidence is lacking, options in care are provided in the clinical standard and the accompanying order sets (if applicable).

Approval Process

Clinical standards are reviewed and approved by hospital committees as deemed appropriate for its intended use. Clinical standards are reviewed as necessary within EBOC at Texas Children’s Hospital. Content Expert Teams are involved with every review and update.

Disclaimer

Practice recommendations are based upon the evidence available at the time the clinical standard was developed. Clinical standards (guidelines, summaries, or pathways) do not set out the standard of care and are not intended to be used to dictate a course of care. Each physician/practitioner must use his or her independent judgment in the management of any specific patient and is responsible, in consultation with the patient and/or the patient’s family, to make the ultimate judgment regarding care.

Version History

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apr 2014</td>
<td>Originally completed</td>
<td></td>
</tr>
<tr>
<td>Apr 2017</td>
<td>Reaffirmed</td>
<td></td>
</tr>
</tbody>
</table>