Inclusion Criteria
- Children with diagnosed or suspected acute invasive fungal rhinosinusitis (AIFS)

**Background**
Acute invasive fungal rhinosinusitis (AIFS) is the invasive infiltration of mycotic organisms in the sinonasal region and angiocentric extension into orbital and intracranial structures. (1) AIFS is a significant source of morbidity and mortality and the population at greatest risk are those that are immunocompromised. (1) Therefore, it is important to identify best practices for diagnosis, imaging, and treatment in order to improve patient outcomes.

**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>
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<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>High</td>
</tr>
<tr>
<td></td>
<td>Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies</td>
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<tr>
<td></td>
<td>Moderate</td>
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<tr>
<td></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></td>
<td>Low</td>
</tr>
<tr>
<td></td>
<td>Evidence for at least 1 critical outcome from observational studies, from RCTs with serious flaws or indirect evidence</td>
</tr>
<tr>
<td></td>
<td>Very Low</td>
</tr>
<tr>
<td></td>
<td>Evidence for at least 1 critical outcome from unsystematic clinical observations or very indirect evidence</td>
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**PICO Question 1:** In pediatric patients with AIFS do negative pathologic surgical margins have improved survival compared to patients with gross removal and positive pathologic margins?

**Recommendation(s):** Weak recommendation with very low quality evidence for achieving negative pathologic surgical margins. (1)

A review of the literature revealed no studies specifically evaluating whether pathologic surgical margins for AIFS improves survival. A retrospective chart review of 25 patients showed that 9/13 patients survived who had a complete resection compared to all 12 patients without a complete resection died. This article defined complete resection as resection to clear margin based on frozen section analysis or surgeon’s report of resection of viable bleeding tissue. This study included adults and children with the average age of 37 years old (18 months - 72 years old).

**PICO Question 2:** In pediatric patients with extensive (cranial neuropathy, orbital, cranial involvement) AIFS, does aggressive surgical debridement (orbital enucleation, removal of cribriform plate) compared to non-aggressive debridement influence survival in patients who have AIFS?

**Recommendation(s):** Weak recommendation with very low quality evidence for offering orbital enucleation as a treatment option to families if treatment teams feel underlying disease prognosis is reasonable. (2)

A review of the literature revealed no studies specifically comparing aggressive vs. non-aggressive surgical debridement in children. A retrospective review of 17 patients with the diagnosis of AIFS were identified, 4 patients with orbital involvement. Three patients who underwent orbital enucleation survived, while 1 patient who did not undergo orbital enucleation died. The average age for a patient with orbital involvement in this study was 27 years old (15-62 years old).
PICO Question 3: In immunocompromised patients, is magnetic resonance imaging (MRI) more sensitive in diagnosing AIFS compared with computed tomography (CT) scan?

Recommendation(s): Strong recommendation with low quality evidence for obtaining MRI over CT scan in immunocompromised patients at risk of AIFS. (3)

A retrospective review of CT and MRI scans of 17 patients were independently reviewed by two neuroradiologists to identify imaging characteristics predictive of AFIS. Patients included had confirmed pathologic diagnosis of AIFS. The conclusion of the study is that MRI scan is more sensitive for detecting early changes of AFIS than CT scan (sensitivity of MRI, 85% and 86%, for both reviewers compared to sensitivity of CT, 57% and 69%). Both imaging modalities have similar specificities.

Critical Points of Evidence*

Evidence Supports
- Attempt to achieve complete surgical resection of diseased tissue (negative pathologic surgical margins). (1) – Weak recommendation, very low quality evidence
- Consider orbital enucleation as a treatment option for patients with AIFS involving the eye, if the treatment teams feel that the underlying disease prognosis is reasonable. (2) – Weak recommendation, very low quality evidence
- Use MRI as a screening modality compared to CT scan for AIFS because of the higher sensitivity and zero radiation exposure. CT scan may be considered for surgical planning and use as an intraoperative image guidance. (3) – Strong recommendation, low quality evidence

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

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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, Scopus
4. Critically Analyze the Evidence
   - 3 nonrandomized studies
5. Summarize the Evidence
   - Materials used in the development of the clinical standard, literature appraisal, and any order sets are maintained in an Acute Invasive Fungal Rhinosinusitis (AIFS) Management 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.

<table>
<thead>
<tr>
<th>Type of Evidence</th>
<th>Quality</th>
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<tbody>
<tr>
<td>Evidence Supports</td>
<td>Strong</td>
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<tr>
<td>Evidence Against</td>
<td>Weak</td>
</tr>
<tr>
<td>Evidence Lacking/Inconclusive</td>
<td>Very Low</td>
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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 diagnosis/management of Acute Invasive Fungal Rhinosinusitis (AIFS) Management 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
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<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Comments</th>
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<td>Jan 2015</td>
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