Inclusion Criteria
- < 1 kg or < 27 weeks of Gestation

Exclusion Criteria
- N/A

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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</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>High</td>
</tr>
<tr>
<td></td>
<td>Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
</tr>
<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>
</tr>
</tbody>
</table>

PICO Question 1: Does systemic antifungal prophylaxis decrease invasive candidiasis and mortality in infants less than 1 kg or < 27 weeks GA?

Recommendation(s): Strong recommendation with high quality evidence to administer systemic antifungal prophylaxis in infants less than 1kg or less than 27 weeks gestational age if the incidence of invasive fungal infections in the TCH NICU exceeds 5 – 10%.

Meta-analysis did not find a statistically significant difference in the rate of death prior to hospital discharge, (typical RR 0.79, 95% CI 0.61 to 1.02) but found a statistically significant reduction in the incidence of invasive fungal infections, (typical RR 0.43, 95% confidence interval (CI) 0.31 to 0.59). Only 2 studies reported neurodevelopmental outcomes. However, the average incidence of invasive fungal infection in the control groups of the trials (16%) was much higher than that generally reported from large cohort studies. (1)

On the basis of current data, fluconazole is the preferred agent of choice, it has been shown to be effective and safe. Systemic Fluconazole prophylaxis is recommended in ELBW infants cared in the units with moderate (5-10%) and high (≥ 10%) rates of invasive candidiasis. (2)
Critical Points of Evidence*

Evidence Supports

- Administer systemic antifungal prophylaxis in infants less than 1kg or less than 27 weeks gestational age if the incidence of invasive fungal infections in the TCH NICU exceeds 5 – 10%. (1-2) Strong recommendation, high 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.

**Prophylactic Antifungal Therapy in Very Low Birth Weight Infants Content Expert Team**
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Sushma Nuthakki, MD, Neonatology
Debra Palazzi, MD, Infectious Disease

**EBP Course Participant and EBOC Support**
Sushma Nuthakki, MD, Neonatology
Andrea Jackson, MBA, RN, Evidence-Based Practice Specialist
Charles Macias, MD, MPH, Medical Director

**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
   - Red Book: Report of the Committee of Infectious Diseases

3. Literature Review of Relevant Evidence
   - Searched: PubMed, Cochrane

4. Critically Analyze the Evidence
   - 1 meta-analysis article, 1 professional organization guidelines, White Papers, etc.

5. Summarize the Evidence
   - Materials used in the development of the clinical standard, literature appraisal, and any order sets are maintained in a Prophylactic Antifungal Therapy in Very Low Birth Weight Infants 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
- **“Evidence Lacking/Inconclusive”** indicates there is insufficient evidence to support or refute an intervention and no conclusion can be drawn from the evidence.

The GRADE criteria were utilized to evaluate the body of evidence used to make practice recommendations. The table below defines how the quality of the evidence is rated and how a strong versus weak recommendation is established. The literature appraisal reflects the critical points of evidence.

<table>
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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 management of Prophylactic Antifungal Therapy in Infants. 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.

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