PICO Question 1: In hospitalized infants and young children at increased risk for respiratory syncytial virus (RSV), does palivizumab (Synagis) prophylaxis along with strict infection control practices compared to strict infection control practices alone decrease the risk of nosocomial RSV infections?

Recommendation(s): Strong recommendation with low quality evidence Palivizumab (Synagis) should not be administered routinely to all hospitalized infants and young children born premature, with chronic lung disease (CLD) or hemodynamically significant heart disease. Continued palivizumab (Synagis) prophylaxis is supported for any child who meets criteria and is admitted to TCH for a disease other than RSV infection after having met criteria for prophylaxis in the outpatient setting. (1-3)

A review of the evidence revealed two observational studies that compared the use of palivizumab (Synagis) coupled with infection control practices to infection control practices alone to determine the effect on the rate of nosocomial infections. Katz 2009 compared the nosocomial RSV infection rates of patients before and after the practice change to administer routine RSV prophylaxis (Synagis or RSV-Ig) monthly during RSV season to all ventilator dependent infants less than 6 months and all infants with congenital heart disease (CHD). The study found that there was not a statistical difference in nosocomial RSV infection rates in the pre- and post-intervention years (rate ratio 3.3; 95% CI 0.16-68, p=0.37). (1) Ohler 2013 evaluated whether the timing of administration of palivizumab (Synagis) would decrease the rate of RSV-related hospitalizations in former NICU patients. Group 1 received monthly inpatient doses of palivizumab (Synagis) during RSV season and Group 2 received one dose of palivizumab (Synagis) before hospital discharge. The study did not find a statistical difference between the hospitalization rates of group 1 and group 2 (4.5% versus 2.1%, respectively; p=0.4564). (2)

The American Academy of Pediatrics Policy Statement on palivizumab (Synagis) prophylaxis supports the adherence to strict infection-control practices for reducing RSV nosocomial infections. The use of palivizumab (Synagis) is not recommended for controlling outbreaks of RSV in the hospital setting or preventing health-care associated RSV infections. (3)

Critical Points of Evidence*

Evidence Supports
- Continued palivizumab (Synagis) prophylaxis is supported for any child who meets criteria and is admitted to TCH for a disease other than RSV infection after having met criteria for prophylaxis in the outpatient setting. (1-3) – Strong recommendation, low quality evidence.

Evidence Against
- Palivizumab (Synagis) should not be administered routinely to all hospitalized infants and young children born premature, with chronic lung disease (CLD) or hemodynamically significant heart disease. (1-3) – Strong recommendation, low quality evidence.

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

- Palivizumab (Synagis) prophylaxis should be administered in the first year of life to infants at increased risk of hospitalization for RSV infection meeting the following criteria:
  1. Infants born before 29 weeks of gestation
  2. Infants born before 32 weeks, 0 days of gestation with chronic lung disease (CLD) defined as > 21% oxygen for at least 28 days after birth.
  3. Infants with hemodynamically significant heart disease, specifically:
     - Infants with cyanotic heart defect with consultation of a cardiologist
     - Infants with acyanotic heart disease who are receiving medication to control congestive heart failure and will require future cardiac surgical procedures
     - Infants with moderate-to-severe pulmonary hypertension
- Palivizumab (Synagis) prophylaxis is not recommended in the 2nd year of life except for children who require at least 28 days of supplemental oxygen after birth and who continue to require medical intervention (supplemental oxygen, chronic corticosteroid or diuretic therapy).
- Continued palivizumab (Synagis) prophylaxis is supported for any child who meets criteria and is admitted to TCH for a disease other than RSV infection after having met criteria for prophylaxis in the outpatient setting.
- Additional populations may be considered for palivizumab (Synagis) prophylaxis given that medical services provide specific data/evidence to the Pharmacy and Therapeutics Committee documenting the benefit of this drug in their patient population. Modifications will be made to the criteria based upon Pharmacy and Therapeutics Committee approval.
<table>
<thead>
<tr>
<th>Hospital</th>
<th>Following 2014 AAP Guidelines?</th>
<th>Dispensing Monthly In-Patient Doses?</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boston Children's Hospital</td>
<td>Yes</td>
<td>Yes</td>
<td>[Personal Communications] “For our oncology and ICU patients, it's up to the attending to determine if they would like to continue in-house. We have also allowed our esophageal atresia patients to continue monthly therapy. Otherwise we are not continuing therapy in-house. Upon discharge though, if the patient has been here for over a month, we will give a discharge dose.”</td>
</tr>
<tr>
<td>Children's Hospital of Philadelphia</td>
<td>Yes</td>
<td>No</td>
<td></td>
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<tr>
<td>Cincinnati Children's Hospital Medical Center</td>
<td>Yes</td>
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<tr>
<td>Children's Hospital Los Angeles</td>
<td>Yes</td>
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<td></td>
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<tr>
<td>Children's Hospital Colorado</td>
<td>Yes</td>
<td>Yes</td>
<td>[Inpatient Use Guideline] Very high risk patients for whom an extended stay is anticipated and for whom a RSV lower respiratory tract infection could result in increased morbidity or mortality may receive palivizumab monthly during RSV season while in the hospital. These patients are less than 1 year of age when the first dose is administered for the season. These are extreme cases, such as cardiac patients with single ventricle and patients who require long-term chronic ventilation. Eligibility is determined by the Attending Provider and the clinical pharmacist.</td>
</tr>
<tr>
<td>Nationwide Children's Hospital</td>
<td>Yes</td>
<td>No</td>
<td></td>
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<tr>
<td>Children's Hospital of Chicago</td>
<td>N/A</td>
<td>N/A</td>
<td>No response</td>
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<td>Children's Hospital of Pittsburgh</td>
<td>Yes</td>
<td>No</td>
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<td>John Hopkins Children's Center</td>
<td>Yes</td>
<td>No</td>
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<tr>
<td>New York-Presbyterian Morgan Stanley-Komansky Children's Hospital</td>
<td>Yes</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Children's National Medical Center</td>
<td>Yes</td>
<td>Yes</td>
<td>[Personal Communications] Patients who meet guidelines would receive monthly doses while in-patient but is limited to the maximum number of doses recommended by the AAP.</td>
</tr>
<tr>
<td>Miami Children's Hospital</td>
<td>No</td>
<td>No</td>
<td>[Personal Communications] New guidelines are pending formal approval.</td>
</tr>
</tbody>
</table>
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.

Palivizumab (Synagis) Prophylaxis in Hospitalized Patients

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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, Cochrane Library, CINAHL
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 a Palivizumab (Synagis) Prophylaxis in Hospitalized Patients 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>
<thead>
<tr>
<th>Recommendation</th>
<th>Type of Evidence</th>
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<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></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 management of Palivizumab (Synagis) Prophylaxis in Hospitalized patients 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 the patient’s family, to make the ultimate judgment regarding care.

Version History

<table>
<thead>
<tr>
<th>Date</th>
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March 2016 Originally completed