

Q-METRIC Sickle Cell Disease Measure 3: Appropriate Antibiotic Prophylaxis for Children with Sickle Cell Disease

Graphics for Section V. Evidence or Other Justification for the Focus of the Measure

Table 4: Evidence Supporting Appropriate Antibiotic Prophylaxis in Children with Sickle Cell Disease

Type of Evidence	Key Findings	Level of Evidence (USPSTF Ranking)	Citations
Clinical guidelines	<p>The goal [of newborn screening] is to identify all newborns with SCD and start them on prophylactic penicillin as early as possible. The recommended regimen is:</p> <ul style="list-style-type: none"> • Newborn to 3 years: Penicillin VK, 125 mg orally twice daily • 3 to 5 years: Penicillin VK, 250 mg orally twice daily (NHLBI, p.75). 	III	National Heart Lung and Blood Institute. The Management of Sickle Cell Disease. National Institutes of Health. Bethesda, MD, 2002.
Comprehensive literature review	<p>In a comprehensive review of the literature on the management of children with sickle cell disease by Kavanagh et al., the authors searched for articles on this topic published between 1995 and 2010. They found eight articles related to penicillin prophylaxis for the prevention of life threatening infection in children with SCD. Of these articles, three provided level I evidence, one provided level II evidence and four provided level III evidence rated using the USPSTF scale.</p>	I	Kavanagh PL, Sprinz PG, Vinci SR, Bauchner H, Wang CJ. Management of children with sickle cell disease: a comprehensive review of the literature. <i>Pediatrics</i> 2011;128(6):e1552-1574.
Meta-analysis	<p>A meta-analysis of three randomized trials found that initiation of penicillin prophylaxis for children with SCD under age 5 years significantly reduced the incidence of pneumococcal infection (OR: 0.37 [95% CI 0.16-0.86]) (Hirst et al., 2010).</p>	I	Hirst C, Owusu-Ofori S. Prophylactic antibiotics for preventing pneumococcal infection in children with sickle cell disease. <i>Cochrane Database of Systematic Reviews</i> 2010; 1-21.

Randomized controlled trial	In a randomized, double-blind, placebo controlled trial, Gaston et al. studied whether daily administration of oral penicillin reduced the incidence of life-threatening infection in children with SCD. In the trial, 215 children under the age of 3 were randomly assigned to receive either 125 mg penicillin or placebo twice daily. The study was ended early because of an 84% reduction in incidence of infection among the intervention group.	I	Gaston MH, Verter JI, Woods G, et al. Prophylaxis with oral penicillin in children with sickle cell anemia. A randomized trial. <i>N Engl J Med</i> 1986;314(25):1593-1599.
Randomized controlled trial	In a randomized, double-blind, placebo controlled trial, Falletta et al. followed 218 children with SCD for an average of 3.2 years. The average age of children at random selection was 5.1 years. All children had received prophylactic penicillin therapy for at least 2 years immediately prior to their 5th birthday and had received the 23-valent pneumococcal vaccine between 2 and 3 years of age and again at the time of randomization. The authors found no significant difference in the incidence of bacteremia or meningitis caused by streptococcus pneumoniae between the treatment and control groups. The authors concluded that prophylactic penicillin therapy can safely be stopped at age 5 for children with SCD who have no history of severe pneumococcal infection or splenectomy.	I	Falletta JM, Woods GM, Verter JI, et al. Discontinuing penicillin prophylaxis in children with sickle cell anemia. Prophylactic Penicillin Study II. <i>J Pediatr</i> 1995; 127(5):685-690.

Note: USPSTF criteria for assessing evidence at the individual study level are as follows: I) Properly powered and conducted randomized controlled trial (RCT); well-conducted systematic review or meta-analysis of homogeneous RCTs. II) Well-designed cohort or case-control analytic study. III) Opinions of respected authorities, based on clinical experience; descriptive studies or case reports; reports of expert committees.