

**SELECTING THE APPROPRIATE FIRST-LINE ANTIBIOTICS FOR TREATING  
UPPER RESPIRATORY TRACT INFECTION:  
A LITERATURE REVIEW**

**ABSTRACT**

The pediatric population belongs to that category of individuals who are always at risk of developing certain illnesses if appropriate care is not taken. It is because of the delicate nature of the children's health and body that makes them quite vulnerable to developing all sorts of illnesses and infections very easily. Moreover, their immune system is also in a developing stage, thus making it more prone to get compromised in case there is an infection severe enough to cause damage within the body. Respiratory illnesses are among the most common infections that pediatric populations are prone to develop during their life. However, with the appropriate management and interventions, these infections could be promptly treated. It all depends upon the physician and their diagnosis - at how promptly it is made to save time. Respiratory illnesses can greatly compromise the living conditions of a child, provided that they cause several complications and also make a child cranky, agitated, and irritable. For this reason, mothers of children are often seen to report to the clinics so that appropriate treatment can be started in their infants that gives them relaxation from their symptoms. However, in this review, we shall explore the possibility of prescribing antibiotics in the pediatric population. The purpose of this study is to bring forward all the considerations that are strictly kept in mind before prescribing

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antibiotics to children since they could very much cause resistance in the individuals too. It is, therefore, very important to keep a check and balance on all the symptoms and the duration of those symptoms before any decision regarding the prescription of antibiotics is made by the physician. This will help prevent all sorts of super-infections, complications, as well as resistance-related incidences in the pediatric population.

**Keywords:** pediatric population, infants, respiratory infections, antibiotics, antibiotics-related resistance.

## INTRODUCTION

Acute Respiratory Infections (ARI) is a very broad topic that needs extensive discussion to be understood properly. Usually, a distinction is made between two categories of infections: upper respiratory tract infections (URIs) and lower respiratory tract infections (LRIs). These divisions delineate the regions within the body where these infections take hold. (1)

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The upper respiratory tract encompasses the network of airways extending from the nostrils to the vocal cords situated within the larynx. This area also includes vital structures like the paranasal sinuses and the middle ear, all of which play integral roles in various respiratory processes of the human body. (2)

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In contrast, the lower respiratory tract encompasses a deeper, more intricate system of airways. It encompasses the continuation of these airways beyond the trachea and bronchi, stretching into the smaller bronchioles and ultimately reaching the delicate alveoli, where the exchange of oxygen and carbon dioxide takes place. (3)

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However, the impact of acute respiratory infections (ARIs) extends beyond the confines of these anatomical divisions. ARIs can have systemic effects on the body, meaning they influence the entire organism rather than just the respiratory tract. This broader influence arises from various

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factors, including the potential for infections to spread beyond their initial point of entry, the presence of harmful microbial toxins, the body's inflammatory response to the infection, and the resultant reduction in lung function. In essence, ARIs can disrupt the body's delicate balance and harmony, affecting not only the respiratory system but also other systems and functions throughout the body. Understanding these dynamics is essential for managing and treating respiratory infections comprehensively. (4)

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With the exception of the neonatal period, acute respiratory infections (ARIs) stand as the most prevalent causes of illness and death among children under the age of five. Regardless of geographic location or economic circumstances, these young souls typically endure a staggering three to six episodes of ARIs every year. Yet, the toll of these infections varies significantly between regions, with the balance between mild and severe cases shifting between high-income and low-income countries. (5)

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The situation takes a particularly distressing turn in developing nations. Here, the severity of lower respiratory tract infections (LRTIs) in children under five reaches alarming levels, resulting in a distressingly high case fatality rate. While medical care can offer some relief, it often falls short in the face of these dire conditions, primarily due to the lack of highly effective antiviral medications. (6)

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The consequences of this global health challenge are heart-wrenching, with approximately 10.8 million children succumbing to its grasp each year. Among these young lives cut short, an estimated 1.9 million can be attributed to ARIs, with a staggering 70 percent of these losses concentrated in the regions of Africa and Southeast Asia. These sobering statistics paint a bleak picture, prompting the World Health Organization (WHO) to estimate that a staggering 2 million children under the age of five lose their lives to pneumonia annually. In the face of this

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staggering toll, the global community must continue its efforts to combat ARIs and their devastating consequences on our most vulnerable population.<sup>(7)</sup>

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## **AN OVERVIEW OF THE MOST COMMON RESPIRATORY INFECTIONS IN THE PEDIATRIC POPULATION**

For the sake of convenience, it is better to discuss the most prevalent respiratory illnesses in the pediatric population to learn more about their incidence and prevalence before going to the treatment side.

A brief overview of the most common respiratory infections is given as follows:

### **Acute Pharyngitis:**

Pharyngitis, a condition marked by the inflammation of the mucous membranes and underlying structures in the throat, is a common ailment that sends children to their primary care physicians in droves. In the United States alone, pediatricians diagnose acute pharyngitis, acute tonsillitis, or streptococcal sore throat in excess of 7 million cases each year. This condition can be triggered by a wide array of viral and bacterial agents, either as an isolated affliction or as part of a more widespread illness.<sup>(8)</sup>

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It is worth noting that the majority of cases involving acute pharyngitis in children are attributable to viral infections, and these tend to be relatively mild and self-limiting. However, among the bacterial culprits, Group A beta-hemolytic streptococcus (GAS) takes center stage as the most significant contributor to acute pharyngitis. Its presence can usher in more severe symptoms and necessitate specific treatment approaches. The landscape of pharyngitis, therefore, presents a diverse array of causes and challenges, making it a common concern in pediatric healthcare.

### **Pneumonia:**

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Pneumonia causes a severe level of disability and complications, particularly when it comes to children under the age of 5. Pneumonia can be categorized in its causes based on both the age of the child and the specific pathogens involved. Neonates, who occupy the earliest phase of life, face the risk of bacterial pathogens that can be transmitted during childbirth. These culprits include group *B streptococci*, *Klebsiella*, *Escherichia coli*, and *Listeria monocytogenes*. Late-onset neonatal pneumonia may also involve *Streptococcus pneumoniae*, *Streptococcus pyogenes*, and *Staphylococcus aureus*.(9)

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As children progress beyond the neonatal period and into infancy and toddlerhood (between 30 days and 2 years old), viruses take center stage as the primary cause of pneumonia. This viral dominance extends to children aged 2 to 5 years old. However, in this age group, we also witness the emergence of bacterial players like *Streptococcus pneumoniae* and *Haemophilus influenzae* type B.(10)

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As children continue to grow, a distinct shift occurs. *Mycoplasma pneumonia* becomes a frequent offender among those aged 5 to 13 years old. Nevertheless, *Streptococcus pneumoniae* remains a formidable adversary, continuing to be the most commonly identified pathogen throughout these formative years.

### **Influenza:**

Infections caused by the influenza virus are an exceedingly common occurrence among children across the world. It is a global health issue of substantial magnitude, with an estimated 90 million cases of influenza annually in children under the age of 5. In the United States alone, the incidence of influenza in children is estimated at 19 per 1,000 per year.(11)

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Interestingly, despite the widespread prevalence of influenza in young children, less than 10% of those under the age of 5 have laboratory-confirmed influenza-related healthcare visits annually.

However, the impact of this virus on healthcare systems remains significant, with an estimated 6% to 12% of U.S. children seeking medical care for influenza or influenza-related illnesses each year. Among those seeking care, young children constitute the largest proportion, with those under 5 years of age being hospitalized due to influenza and related conditions at a rate of 1,000 per 100,000 person-years.<sup>(12)</sup>

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On a global scale, the toll of influenza-related lower respiratory tract infections in children is particularly sobering. It is estimated that approximately 28,000 children under the age of 18 succumb to these infections each year, with the majority of these tragic losses occurring among children under 4 years of age. The widespread impact of influenza on the health and well-being of young children underscores the urgency of preventive measures and the need for effective management of this formidable respiratory virus.<sup>(13)</sup>

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## **THE ROLE OF ANTIBIOTICS IN THE MANAGEMENT AND TREATMENT PROTOCOLS FOR RESPIRATORY ILLNESSES IN THE PEDIATRIC POPULATION**

Even in an era marked by remarkable strides in the field of medical science, the treatment of infectious diseases remains a formidable challenge. This enduring difficulty is primarily attributable to the emergence of antimicrobial resistance (AMR), a phenomenon that not only looms as a grave threat to global health but also casts shadows over food security and economic development.<sup>(14)</sup>

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In the year 2019, the world bore witness to the devastating consequences of bacterial AMR, with more than 4.95 million lives claimed by diseases in which antimicrobial resistance played a contributing role. Among these grim statistics, 1.27 million deaths could be directly attributed to the insidious effects of AMR. These numbers underscore the urgency of addressing this growing

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crisis, which jeopardizes both individual lives and the broader well-being of societies around the world.(15)

However, despite the risk of antibiotic resistance looming at all times, respiratory diseases continue to cast a significant shadow on global health, particularly affecting the most vulnerable of all young children. To resolve the problem of managing and treating respiratory infections appropriately, the World Health Organization (WHO) took a significant step by introducing the Integrated Management of Childhood Illness (IMCI) guidelines. These guidelines serve as a crucial tool to assist healthcare professionals in diagnosing and treating the primary causes of mortality in under-five children. Since its inception, IMCI has been adopted in more than 75 countries, making a substantial impact on child health worldwide.(16)

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Designed to be user-friendly and applicable in primary care settings with limited equipment and resources, a complete IMCI assessment typically takes around 8 to 12 minutes. Among the major causes of mortality in under-fives, pneumonia stands out as the leading culprit. However, there is evidence to suggest that mortality resulting from lower respiratory diseases, such as asthma, often goes underreported.(17)

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The primary method for diagnosing pneumonia in primary care across the globe relies heavily on clinical signs, such as cough and rapid breathing. IMCI simplifies the diagnosis of pneumonia by utilizing straightforward clinical signs like cough and fast breathing, providing a practical approach for healthcare providers. When specific criteria are met, the guidelines recommend empiric antibiotic treatment. However, this approach has raised concerns that pneumonia might be over diagnosed, leading to unnecessary antibiotic prescriptions. This is because IMCI, while sensitive, lacks specificity when it comes to diagnosing pneumonia.(18)

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It is important to recognize that respiratory diseases in young children encompass a broad spectrum of conditions, each with its own set of overlapping symptoms. This range includes self-limiting viral infections, bacterial infections, and even non-communicable diseases, further complicating the diagnostic landscape. As healthcare professionals strive to provide the best care for these young patients, navigating this complex terrain remains an ongoing challenge.

**Problems With Antibiotic Prescriptions:**

However, a recent report from the World Health Organization (WHO) has pinpointed the issue of unnecessary antibiotic prescriptions as a crucial concern in the battle against the global threat of antimicrobial resistance. This study, in particular, shed light on a troubling trend where nearly half of children diagnosed with viral upper respiratory tract infections (URTI) were prescribed antibiotics. In the United States, a survey involving 5,700 children and teenagers who sought care for acute URIs revealed a similarly troubling pattern, with approximately half of them receiving antibiotics when they were not warranted.<sup>(19)(20)</sup>

While data regarding the global extent of unnecessary antibiotic prescriptions remains somewhat limited, it is plausible that the issue is even more pronounced in countries where over-the-counter antibiotic sales are not regulated—a facet not directly addressed in this study.

Qualitative insights gleaned from places like Kyrgyzstan and Uganda provide valuable context, showcasing a scenario where caregivers frequently bypass repeat consultations and head straight to the pharmacy for medications with similar symptoms. They often seek the same medicine prescribed during their initial visit, driven by a desire to save both time and money.<sup>(21)</sup>

This troubling chain of events underscores how an initial inappropriate prescription of antibiotics can set in motion a cascade of unnecessary antibiotic use. It also creates an expectation among caregivers that antibiotics are the go-to treatment, even for viral infections. The implications of

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such practices on antimicrobial resistance are significant, highlighting the urgent need for strategies to address this issue on a global scale.

When it comes to children diagnosed with viral respiratory tract infections (VRTIs), those who are not prescribed antibiotics do not show elevated rates of bacterial infections or a higher likelihood of returning to the physician for further care. Similarly, children who are administered first-line antibiotics for conditions like otitis media or pharyngitis do not experience a delayed resolution of symptoms compared to those receiving second-line antibiotic agents. This suggests that the judicious use of antibiotics, especially in cases of viral infections, does not necessarily lead to better outcomes or a quicker recovery for these young patients.(22)(15)

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## CONCLUSION

Respiratory illnesses pose a great risk to the pediatric population, mainly because of their serious nature. The affected children are more likely to suffer from the complications of these illnesses if they are not promptly treated for them. However, prescribing antibiotics is also not always the smartest choice for children. It is seen in several practices that pediatricians unnecessarily prescribe antibiotics even when they are not needed. This could lead to even more grave consequences, such as the development of antimicrobial resistance in children. Therefore, it is best to stay updated with the guidelines to prescribe only the most appropriate of all medications to the children, and only as per the need.

## REFERENCES

1. Simoes EAF, Cherian T, Chow J, Shahid-Salles SA, Laxminarayan R, John TJ. Acute Respiratory Infections in Children. In: Jamison DT, Breman JG, Measham AR, Alleyne G, Claeson M, Evans DB, et al., editors. Disease Control Priorities in Developing Countries

[Internet]. 2nd ed. Washington (DC): The International Bank for Reconstruction and Development / The World Bank; 2006 [cited 2023 Oct 7]. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK11786/>

2. Thomas M, Bomar PA. Upper Respiratory Tract Infection. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 [cited 2023 Oct 7]. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK532961/>

3. Mahashur A. Management of lower respiratory tract infection in outpatient settings: Focus on clarithromycin. *Lung India Off Organ Indian Chest Soc.* 2018;35(2):143–9.

4. MacDonald NE. Pediatric infections. *Can J Infect Dis.* 1992;3(2):75–7.

5. Newbould L, Campbell SM, Edwards G, Morris RL, Hayward G, Hughes EC, et al. Respiratory infections in children: an appropriateness study of when parents should home care or seek medical help. *Br J Gen Pract.* 2020 Dec 15;71(703):e140–7.

6. Bhurtel R, Pokhrel RP, Kalakheti B. Acute Respiratory Infections among Under-five Children Admitted in a Tertiary Hospital of Nepal: A Descriptive Cross-sectional Study. *JNMA J Nepal Med Assoc.* 2022 Jan;60(245):17–21.

7. Dagne H, Andualem Z, Dagne B, Taddese AA. Acute respiratory infection and its associated factors among children under-five years attending pediatrics ward at University of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia: institution-based cross-sectional study. *BMC Pediatr.* 2020 Feb 28;20:93.

8. Gerber MA. Diagnosis and Treatment of Pharyngitis in Children. *Pediatr Clin North Am.* 2005 Jun;52(3):729–47.

9. Ebeledike C, Ahmad T. Pediatric Pneumonia. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 [cited 2023 Oct 7]. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK536940/>
10. Popovsky EY, Florin TA. Community-Acquired Pneumonia in Childhood. *Encycl Respir Med*. 2022;119–31.
11. Nayak J, Hoy G, Gordon A. Influenza in Children. *Cold Spring Harb Perspect Med*. 2021 Jan 4;11(1):a038430.
12. Willis GA, Preen DB, Richmond PC, Jacoby P, Effler PV, Smith DW, et al. The impact of influenza infection on young children, their family and the health care system. *Influenza Other Respir Viruses*. 2019 Jan;13(1):18–27.
13. Hoy G, Kuan G, López R, Sánchez N, López B, Ojeda S, et al. The Spectrum of Influenza in Children. *Clin Infect Dis Off Publ Infect Dis Soc Am*. 2023 Feb 8;76(3):e1012–20.
14. Mustafa ZU, Khan AH, Salman M, Syed Sulaiman SA, Godman B. Antimicrobial Utilization among Neonates and Children: A Multicenter Point Prevalence Study from Leading Children's Hospitals in Punjab, Pakistan. *Antibiotics*. 2022 Aug 4;11(8):1056.
15. Medernach RL, Logan LK. The Growing Threat of Antibiotic Resistance in Children. *Infect Dis Clin North Am*. 2018 Mar;32(1):1–17.
16. The Integrated Management of Childhood Illness. In: *Guideline: Assessing and Managing Children at Primary Health-Care Facilities to Prevent Overweight and Obesity in the Context of the Double Burden of Malnutrition: Updates for the Integrated Management of Childhood Illness (IMCI)* [Internet]. World Health Organization; 2017 [cited 2023 Oct 7]. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK487907/>

17. Kilov K, Hildenwall H, Dube A, Zadutsa B, Banda L, Langton J, et al. Integrated Management of Childhood Illnesses (IMCI): a mixed-methods study on implementation, knowledge and resource availability in Malawi. *BMJ Paediatr Open*. 2021 Apr 30;5(1):e001044.
18. Johansson EW, Nsona H, Carvajal-Aguirre L, Amouzou A, Hildenwall H. Determinants of Integrated Management of Childhood Illness (IMCI) non-severe pneumonia classification and care in Malawi health facilities: Analysis of a national facility census. *J Glob Health*. 7(2):020408.
19. 160518\_Final paper\_with cover.pdf [Internet]. [cited 2023 Oct 7]. Available from: [https://amr-review.org/sites/default/files/160518\\_Final%20paper\\_with%20cover.pdf](https://amr-review.org/sites/default/files/160518_Final%20paper_with%20cover.pdf)
20. Antimicrobial resistance: global report on surveillance [Internet]. [cited 2023 Oct 7]. Available from: <https://www.who.int/publications-detail-redirect/9789241564748>
21. Havers FP, Hicks LA, Chung JR, Gaglani M, Murthy K, Zimmerman RK, et al. Outpatient Antibiotic Prescribing for Acute Respiratory Infections During Influenza Seasons. *JAMA Netw Open*. 2018 Jun 1;1(2):e180243.
22. Kozyrskyj AL, Dahl ME, Chateau DG, Mazowita GB, Klassen TP, Law BJ. Evidence-based prescribing of antibiotics for children: role of socioeconomic status and physician characteristics. *CMAJ Can Med Assoc J*. 2004 Jul 20;171(2):139-45.