

**ANTIBIOTIC RESISTANCE IN CHILDREN AND STRATEGIES FOR
RATIONAL ANTIBIOTIC THERAPY**

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Abstract: *This scientific article analyzes the relevance of the growing problem of antibiotic resistance (antimicrobial resistance) in pediatric practice, which is largely driven by irrational and unjustified use of antibiotics, as well as its etiological factors and clinical-epidemiological consequences. In recent years, antibiotics have frequently been prescribed in pediatrics for conditions such as respiratory tract infections, acute otitis media, tonsillopharyngitis, bronchitis, and intestinal infections, often without laboratory confirmation and even in cases where viral etiology is highly probable. Such an approach promotes the emergence of resistant microbial strains, reduces treatment effectiveness, increases the duration and recurrence of disease, contributes to a higher rate of complications, and raises the need for inpatient management. The article highlights the pathogenetic mechanisms of antibiotic resistance, including β -lactamase production, modification of bacterial cell wall and ribosomal structures, activation of efflux pumps, and biofilm formation, from a scientific perspective. Furthermore, modern strategies for rational antibiotic therapy in children are discussed in detail, including an etiology-based approach, strict adherence to clinical guidelines, prioritization of narrow-spectrum agents, individualized dosing and treatment duration, restriction of uncontrolled antibiotic sales, and implementation of antimicrobial stewardship programs in pediatric healthcare. In addition, the article identifies major socio-organizational factors that contribute to the increasing resistance, such as parents' misconceptions about antibiotics, physicians' excessive precautionary prescribing, limited access to rapid diagnostic tools, and insufficient pharmaceutical regulation. As a result, the article concludes that reducing antibiotic resistance among children requires not only pharmacological interventions but also comprehensive strategies involving healthcare*

system reforms, education and prevention measures, improved laboratory diagnostics, and effective public awareness initiatives.

Keywords: *antibiotic resistance, antimicrobial resistance, pediatrics, rational antibiotic therapy, antimicrobial stewardship, inappropriate antibiotic use, narrow-spectrum antibiotics, β -lactamase, biofilm, empirical therapy, clinical guidelines, laboratory diagnostics, antibiotic stewardship programs, infectious diseases, prevention*

Introduction: In recent years, antibiotic resistance, widely referred to as antimicrobial resistance (AMR), has emerged as one of the most critical threats to global public health and healthcare systems. Although antibiotics remain among the most effective interventions for the treatment of bacterial infections, their irrational, inappropriate, and unjustified use has significantly accelerated the selection and spread of resistant microorganisms, thereby narrowing therapeutic options and undermining clinical outcomes. The World Health Organization (WHO) recognizes AMR as a major medical, social, and economic challenge of the 21st century, with direct implications for infection control, patient safety, and healthcare sustainability. In pediatric clinical practice, the issue of antibiotic use requires special attention due to the high burden of infectious diseases in children, the immaturity of immune defense mechanisms, and the frequent occurrence of respiratory infections, acute otitis media, tonsillopharyngitis, bronchitis, and gastrointestinal infections. In many settings, antibiotics are still prescribed empirically, without etiological confirmation or microbiological susceptibility testing. However, a substantial proportion of acute respiratory illnesses in children are viral in origin, and antibiotic therapy in such cases does not improve clinical recovery. Instead, unnecessary exposure to antimicrobials increases selective pressure, contributing to the emergence of resistant bacterial strains and altering the child's microbiome. The development of antibiotic resistance is driven by several well-established biological mechanisms, including β -lactamase production, structural modifications of bacterial cell wall targets and ribosomal binding sites, activation of efflux pump systems, and enhanced biofilm formation. Current evidence indicates a rising prevalence of multidrug-resistant (MDR) pathogens frequently encountered in pediatric populations, including *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Staphylococcus aureus*, and members of the Enterobacteriaceae family. The increasing resistance among these organisms complicates treatment decisions, reduces the effectiveness of first-line narrow-spectrum agents, and often necessitates the use of broader-spectrum antibiotics associated with higher costs and a greater risk of adverse events. Importantly, irrational antibiotic prescribing in children is not only associated with reduced therapeutic efficacy but also contributes to a range of clinically significant complications, including hypersensitivity reactions, antibiotic-associated diarrhea, intestinal dysbiosis, prolonged disease course,



and increased recurrence rates. In addition, inappropriate antibiotic use imposes a substantial economic burden on healthcare systems by increasing outpatient and inpatient costs, length of hospital stay, and the need for advanced diagnostic and therapeutic resources. At present, international guidelines emphasize that reducing AMR in pediatrics requires comprehensive, evidence-based strategies. These include strict adherence to clinical protocols, prioritization of narrow-spectrum antibiotics whenever appropriate, expansion of laboratory diagnostics and antimicrobial susceptibility testing, individualized dose optimization based on age and body weight, standardized treatment duration, and implementation of antimicrobial stewardship programs. Moreover, regulatory measures aimed at restricting non-prescription antibiotic sales and strengthening pharmaceutical oversight are considered essential components of AMR containment policies. Therefore, an in-depth analysis of antibiotic resistance in children and the development of rational antibiotic therapy strategies remain key priorities in contemporary pediatric research and clinical practice.

Main part: Antibiotic resistance in children has become a major concern not only in clinical pediatrics but also in the broader context of public health and the sustainability of healthcare systems. Historically, antibiotics have been among the most effective therapeutic tools for the management of bacterial infections and have played a decisive role in reducing childhood mortality from severe conditions such as bacterial pneumonia, meningitis, sepsis, pyelonephritis, and other life-threatening infectious diseases. However, widespread, often uncontrolled and clinically unjustified antibiotic use has accelerated the emergence and dissemination of antimicrobial resistance, ultimately complicating treatment outcomes. This issue is particularly critical in pediatrics, given the high frequency of infectious illnesses in children, the relative immaturity of immune defenses, the self-limiting nature of many common infections, and the persistent pressure from caregivers who frequently expect antibiotics as a “rapid solution.”

In everyday clinical practice, antibiotics are commonly prescribed for acute respiratory tract infections, bronchitis, pharyngitis, otitis media, and sinusitis. A substantial proportion of these conditions are viral in origin; nevertheless, antibiotics are still frequently used for perceived prevention of complications or to shorten recovery time. Such an approach does not significantly improve clinical outcomes but substantially increases selective pressure on microbial populations. Under selective pressure, not only classical pathogens but also members of the normal commensal flora may acquire resistant traits. Consequently, the current infectious episode becomes more difficult to treat, and future infections may no longer respond to standard first-line agents. Moreover, repeated and inappropriate antibiotic exposure in children can disrupt the intestinal microbiota, increasing the risk of dysbiosis, antibiotic-associated diarrhea, hypersensitivity reactions, and immunological alterations.



The development of antimicrobial resistance is strongly linked to evolutionary adaptation mechanisms, mediated either by spontaneous genetic mutations or by horizontal gene transfer. Bacteria can exchange resistance determinants through plasmids, transposons, and integrons, enabling rapid dissemination of resistance genes across species. This process is particularly relevant in pediatrics because the intestinal microbiome of children is dynamic and vulnerable to perturbations, facilitating the spread of resistant determinants among different bacterial populations. The production of β -lactamases remains one of the most clinically significant mechanisms, reducing the efficacy of β -lactam antibiotics such as penicillins and cephalosporins. In addition, alterations in penicillin-binding proteins (PBPs) contribute to decreased susceptibility of *Streptococcus pneumoniae* to β -lactams. Resistance to macrolides, tetracyclines, and fluoroquinolones is often associated with modifications of ribosomal targets, while activation of efflux pump systems can lower intracellular antibiotic concentrations to subtherapeutic levels. Biofilm formation further enhances bacterial survival by creating a protective microenvironment that reduces antibiotic penetration and limits host immune activity, thereby contributing to persistent and recurrent infections.

From a clinical standpoint, the most relevant resistant pathogens in pediatric populations include *Streptococcus pneumoniae*, *Haemophilus influenzae*, staphylococci, enterococci, and members of the Enterobacteriaceae family. In recent years, increasing prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA), extended-spectrum β -lactamase (ESBL)-producing *Escherichia coli* and *Klebsiella pneumoniae*, and carbapenem-resistant Enterobacterales (CRE) has been documented. Infections caused by these organisms are frequently prolonged, associated with a higher risk of complications, and more likely to require inpatient management. Such cases often necessitate the use of so-called “reserve” or last-line antibiotics. Nevertheless, in pediatric settings these agents must be used with caution due to age-related pharmacokinetic considerations, limited safety data for certain drug classes, and the increased risk of adverse drug reactions. Furthermore, resistant infections often require advanced laboratory diagnostics and continuous clinical monitoring, which increases the overall cost of care and places an additional burden on healthcare resources.

Rational antibiotic therapy is therefore a cornerstone of improving clinical outcomes in children, slowing the spread of resistance, and ensuring medication safety. The first essential step in rational prescribing is the establishment of clear clinical indications for antibiotic initiation. This involves careful evaluation of the likelihood of bacterial etiology, integration of laboratory markers such as leukocytosis, C-reactive protein, and procalcitonin, and assessment of clinical symptom dynamics. Antibiotics should not be used for uncomplicated viral infections; instead, such patients should undergo active clinical follow-up to detect possible bacterial complications. A second critical step is



selecting empiric antibiotics based on local epidemiological data and resistance patterns. The same clinical diagnosis may be associated with different dominant pathogens and resistance rates across regions, and therefore antibiotic selection should be tailored to real-world local conditions rather than relying solely on generalized recommendations.

A fundamental principle of rational prescribing is prioritizing narrow-spectrum antibiotics whenever clinically appropriate. Unnecessary use of broad-spectrum agents causes substantial disruption of the gut microbiota and intensifies selection of resistant strains. In addition, antibiotic dosing must be individualized based on the child's age, body weight, renal and hepatic function, infection severity, and the pharmacokinetic/pharmacodynamic properties of the selected drug. Subtherapeutic dosing represents one of the most dangerous contributors to resistance development because it fails to achieve bacterial eradication and instead promotes microbial adaptation. Treatment duration must also be evidence-based. In routine practice, antibiotics are often prescribed for unnecessarily prolonged courses, which increases adverse events and resistance risk. Modern clinical guidelines increasingly support shorter courses (commonly 5–7 days) for many pediatric infections, with extended therapy reserved only for specific severe conditions.

Laboratory diagnostics play a central role in optimizing antibiotic therapy in pediatric care. Pathogen identification and antimicrobial susceptibility testing facilitate accurate antibiotic selection and allow transition from empiric therapy to targeted therapy. However, in many real-world settings, microbiological testing may be limited, unavailable, or delayed. For this reason, the broader implementation of rapid diagnostic tools, including point-of-care tests, molecular assays, and antigen detection methods, is a key component of rational antibiotic stewardship. Rapid tests for viral pathogens, such as influenza and respiratory syncytial virus (RSV), are particularly valuable for reducing unnecessary antibiotic prescriptions.

Antimicrobial stewardship programs have been internationally recognized as effective systems for promoting appropriate antibiotic use in pediatric healthcare facilities. These programs typically incorporate standardized prescribing algorithms, clinical audit and feedback, continuous physician education, antibiotic consumption monitoring, and epidemiological surveillance of resistance trends. Evidence from multiple settings indicates that stewardship interventions can reduce overall antibiotic use, limit inappropriate broad-spectrum prescribing, and slow the spread of resistant organisms. Importantly, the social determinants of antibiotic prescribing must also be addressed. Caregivers often hold misconceptions that antibiotics are essential for recovery, while clinicians may prescribe defensively due to concerns related to legal liability, patient expectations, and time constraints in high-volume clinical environments. In this context, public education and parental counseling are essential, particularly regarding the

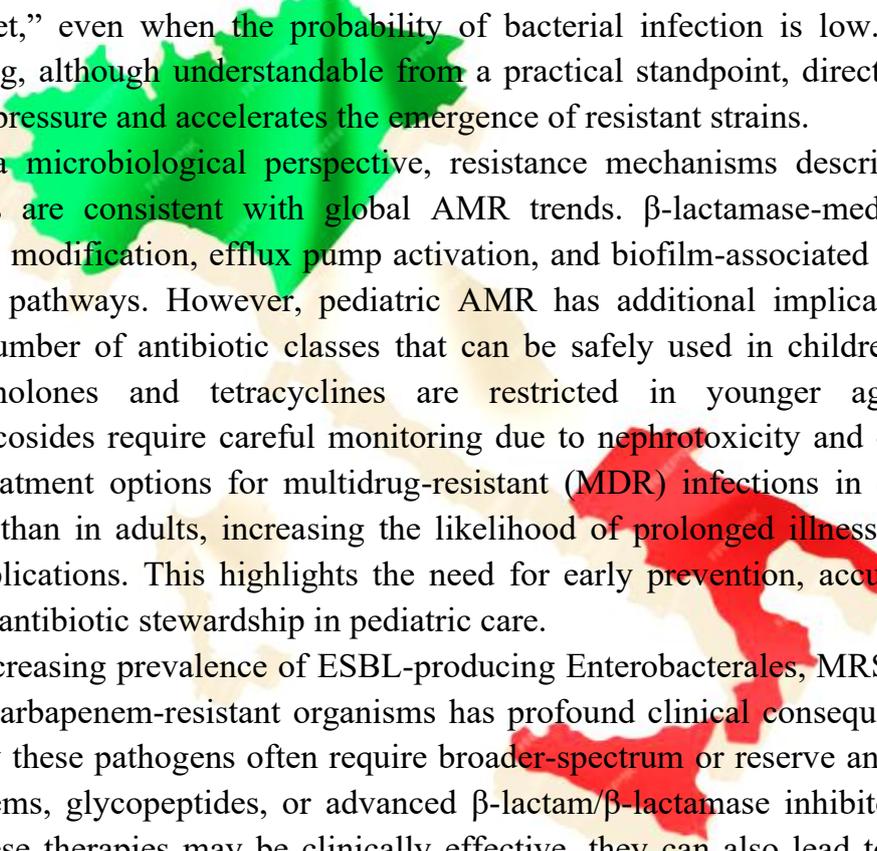
distinction between viral and bacterial infections and the potential harms associated with unnecessary antibiotic exposure.

Unregulated antibiotic access and self-medication represent additional drivers of resistance. In some regions, antibiotics can still be obtained without a prescription, enabling caregivers to treat children without medical supervision and often with inappropriate dosing and treatment duration. This practice significantly increases the risk of adverse drug events and accelerates resistance selection. Therefore, strengthening regulatory control over antibiotic distribution, enforcing prescription-only policies, and improving pharmaceutical oversight constitute key legal and policy measures within AMR containment strategies. In parallel, healthcare systems should promote standardized prescribing based on evidence-based clinical protocols, provide continuous professional development for clinicians, and develop local resistance surveillance maps to guide empiric treatment decisions.

Preventive interventions also play a critical role in reducing antibiotic resistance in children. Vaccination decreases the incidence of bacterial infections and related complications, thereby reducing the overall need for antibiotics. Pneumococcal and Haemophilus influenzae type b (Hib) vaccines have been shown to reduce cases of acute otitis media, pneumonia, and meningitis, contributing to lower antibiotic consumption. Influenza vaccination may also reduce secondary bacterial complications associated with viral respiratory infections. Additionally, infection prevention and control measures—including adherence to hygiene standards, strengthening infection control in childcare facilities, promoting hand hygiene, and isolating symptomatic children—are simple yet highly effective strategies for reducing transmission of infectious diseases and consequently lowering antibiotic demand.

Overall, antibiotic resistance in children is a multifactorial and complex challenge requiring a coordinated and comprehensive response. Effective mitigation depends on the integration of rational antibiotic prescribing guided by clinical protocols, expanded diagnostic capacity, implementation of antimicrobial stewardship programs, strengthened pharmaceutical and regulatory frameworks, and improved antibiotic literacy among caregivers and healthcare professionals. Only through such a multidisciplinary approach can the spread of resistant strains in pediatric populations be slowed, the clinical effectiveness of antibiotics preserved, and the health of future generations safeguarded.

Discussion: The findings and concepts discussed in this article confirm that antimicrobial resistance (AMR) in children is not merely a microbiological phenomenon, but rather a complex clinical, organizational, behavioral, and regulatory challenge. In pediatric populations, the burden of infectious diseases is high, and the frequency of antibiotic exposure is substantially greater than in many adult groups. This creates a unique environment in which resistant organisms can emerge early, persist within the

child's microbiome, and spread across households, daycare institutions, and healthcare facilities. Importantly, pediatric AMR is not limited to hospital settings; community-acquired resistant infections are increasingly reported, indicating that resistance containment strategies must extend beyond inpatient care. A major driver of AMR in pediatrics remains the persistent overprescribing of antibiotics for conditions with predominantly viral etiology. Upper respiratory tract infections, acute bronchitis, and non-specific febrile illnesses represent the most frequent indications for antibiotic prescriptions in children, despite limited evidence of bacterial involvement in most cases. This pattern is reinforced by multiple interacting factors, including diagnostic uncertainty, limited access to rapid testing, parental expectations, and time constraints in outpatient practice. In many clinical encounters, antibiotics are prescribed as a perceived "safety net," even when the probability of bacterial infection is low. Such defensive prescribing, although understandable from a practical standpoint, directly contributes to selective pressure and accelerates the emergence of resistant strains.

From a microbiological perspective, resistance mechanisms described in pediatric pathogens are consistent with global AMR trends. β -lactamase-mediated resistance, target-site modification, efflux pump activation, and biofilm-associated tolerance remain dominant pathways. However, pediatric AMR has additional implications due to the limited number of antibiotic classes that can be safely used in children. For example, fluoroquinolones and tetracyclines are restricted in younger age groups, and aminoglycosides require careful monitoring due to nephrotoxicity and ototoxicity. As a result, treatment options for multidrug-resistant (MDR) infections in children may be narrower than in adults, increasing the likelihood of prolonged illness, hospitalization, and complications. This highlights the need for early prevention, accurate diagnostics, and strict antibiotic stewardship in pediatric care.

The increasing prevalence of ESBL-producing Enterobacterales, MRSA, and, in some regions, carbapenem-resistant organisms has profound clinical consequences. Infections caused by these pathogens often require broader-spectrum or reserve antibiotics, such as carbapenems, glycopeptides, or advanced β -lactam/ β -lactamase inhibitor combinations. While these therapies may be clinically effective, they can also lead to higher rates of adverse drug reactions, increased healthcare costs, and further selection of resistant organisms. In pediatrics, these risks are amplified due to age-related pharmacokinetic variability, dosing complexity, and the vulnerability of the developing microbiome. Consequently, the clinical challenge is not only to treat resistant infections effectively, but also to prevent the cycle of escalating antibiotic exposure that fuels future resistance.

An important and increasingly recognized aspect of pediatric antibiotic exposure is its impact on the gut microbiota and immune development. Early-life antibiotic use has been associated with microbiome disruption, which may persist for months or years and

potentially influence long-term health outcomes. Although causal relationships remain under investigation, growing evidence suggests links between repeated antibiotic exposure and increased risk of allergic diseases, metabolic disorders, and inflammatory conditions. From a public health perspective, this adds another layer of justification for minimizing unnecessary antibiotic prescriptions, especially in early childhood.

The discussion of rational antibiotic therapy emphasizes that stewardship is not simply about reducing antibiotic use; it is about optimizing antibiotic decision-making. This includes selecting the right agent, at the right dose, for the right duration, and for the right indication. The prioritization of narrow-spectrum antibiotics remains a key principle, yet it requires confidence in diagnosis and awareness of local resistance patterns. In settings where microbiological diagnostics are limited, clinicians often rely on empirical treatment. While empirical therapy is sometimes unavoidable, it should be guided by local epidemiological data and updated resistance surveillance. Without such information, empirical prescribing becomes inconsistent and may unintentionally promote resistance through inappropriate antibiotic selection.

Rapid diagnostics represent one of the most effective tools for improving pediatric antibiotic prescribing. Point-of-care tests for streptococcal pharyngitis, influenza, RSV, and biomarkers such as C-reactive protein and procalcitonin can reduce diagnostic uncertainty and support evidence-based decisions. Nevertheless, these tools are not universally available, and in some healthcare systems their use is limited by cost, infrastructure, or lack of training. Expanding diagnostic capacity should therefore be considered a strategic investment in AMR control. Importantly, diagnostic tools must be integrated into clinical pathways, rather than used sporadically, to achieve measurable reductions in unnecessary antibiotic prescribing.

Antimicrobial stewardship programs (ASPs) are internationally recognized as essential for AMR containment, and pediatric-focused ASPs have demonstrated effectiveness in both hospital and outpatient settings. Successful programs typically combine guideline development, audit and feedback, antibiotic restriction policies, education, and monitoring of antibiotic consumption. In pediatrics, stewardship also requires age-specific protocols and dosing guidance, as well as multidisciplinary collaboration between pediatricians, infectious disease specialists, clinical pharmacists, microbiologists, and infection control teams. Where stewardship programs are implemented systematically, reductions in broad-spectrum antibiotic use, improved guideline adherence, and decreased rates of healthcare-associated resistant infections have been reported.

However, stewardship interventions alone may not be sufficient without addressing the broader regulatory and societal context. Non-prescription access to antibiotics, weak pharmaceutical oversight, and inconsistent enforcement of prescription-only regulations



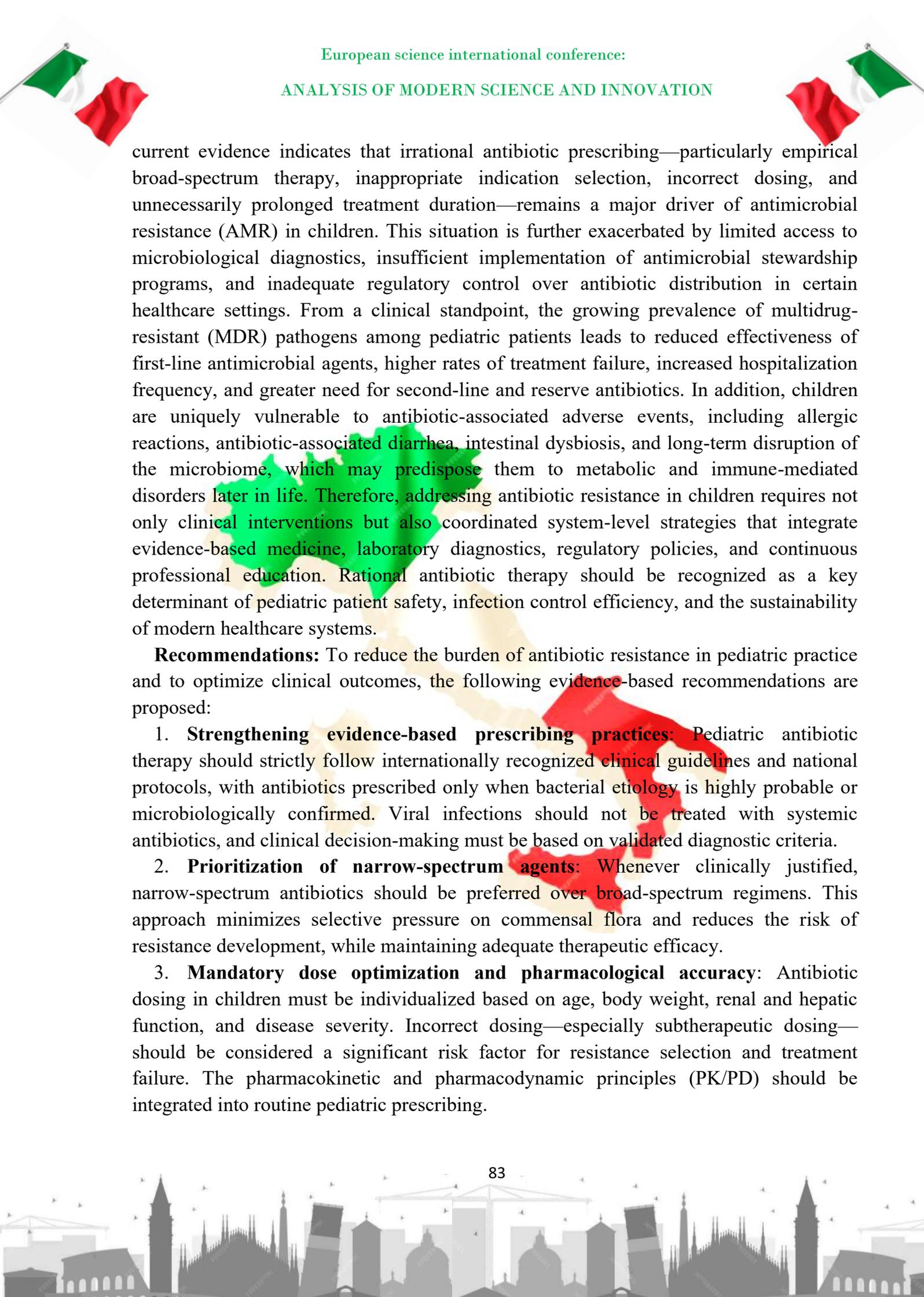
remain major barriers in many regions. The availability of antibiotics without appropriate medical supervision increases self-medication, incomplete courses, incorrect dosing, and inappropriate antibiotic selection. These behaviors accelerate resistance and increase the risk of adverse drug events in children. Strengthening legal frameworks for antibiotic distribution, ensuring pharmacy compliance, and implementing regulatory monitoring systems are therefore critical components of a comprehensive AMR strategy. In addition, national and regional policies should support surveillance systems that track resistance trends and antibiotic consumption, enabling evidence-based public health interventions.

Public education is another essential element in AMR containment. Caregivers often perceive antibiotics as universally beneficial and may equate antibiotic prescribing with high-quality medical care. In pediatric practice, such expectations can influence prescribing behavior, especially in high-demand outpatient environments. Educational interventions should focus on improving antibiotic literacy, clarifying the differences between viral and bacterial infections, and explaining the potential harms of unnecessary antibiotic exposure. Communication strategies that emphasize safety, symptom management, and follow-up plans can reduce caregiver dissatisfaction when antibiotics are not prescribed. This approach supports a more rational healthcare culture while maintaining trust between clinicians and families.

Preventive strategies, particularly vaccination, play a crucial role in reducing the overall burden of bacterial infections and limiting antibiotic demand. Pneumococcal and Hib vaccination programs have significantly reduced invasive bacterial disease, pneumonia, and otitis media in children, which indirectly contributes to decreased antibiotic consumption and slower resistance development. Influenza vaccination also reduces the incidence of secondary bacterial infections. In addition, infection prevention and control measures in daycare centers, schools, and healthcare facilities—such as hand hygiene promotion, respiratory etiquette, and isolation of symptomatic children—remain cost-effective interventions for reducing transmission of infections.

Overall, the discussion highlights that pediatric AMR requires a multi-layered response that integrates clinical stewardship, diagnostic strengthening, regulatory enforcement, preventive vaccination programs, and community education. The pediatric population represents both a vulnerable group and a critical target for long-term AMR control, as early-life antibiotic exposure may shape resistance patterns at both individual and community levels. Therefore, improving rational antibiotic therapy in children is not only a clinical necessity but also a strategic investment in future public health and the preservation of antibiotic effectiveness.

Conclusion: Antibiotic resistance in pediatric populations represents a rapidly escalating clinical and public health concern, significantly complicating the management of common childhood infections and increasing the risk of unfavorable outcomes. The



current evidence indicates that irrational antibiotic prescribing—particularly empirical broad-spectrum therapy, inappropriate indication selection, incorrect dosing, and unnecessarily prolonged treatment duration—remains a major driver of antimicrobial resistance (AMR) in children. This situation is further exacerbated by limited access to microbiological diagnostics, insufficient implementation of antimicrobial stewardship programs, and inadequate regulatory control over antibiotic distribution in certain healthcare settings. From a clinical standpoint, the growing prevalence of multidrug-resistant (MDR) pathogens among pediatric patients leads to reduced effectiveness of first-line antimicrobial agents, higher rates of treatment failure, increased hospitalization frequency, and greater need for second-line and reserve antibiotics. In addition, children are uniquely vulnerable to antibiotic-associated adverse events, including allergic reactions, antibiotic-associated diarrhea, intestinal dysbiosis, and long-term disruption of the microbiome, which may predispose them to metabolic and immune-mediated disorders later in life. Therefore, addressing antibiotic resistance in children requires not only clinical interventions but also coordinated system-level strategies that integrate evidence-based medicine, laboratory diagnostics, regulatory policies, and continuous professional education. Rational antibiotic therapy should be recognized as a key determinant of pediatric patient safety, infection control efficiency, and the sustainability of modern healthcare systems.

Recommendations: To reduce the burden of antibiotic resistance in pediatric practice and to optimize clinical outcomes, the following evidence-based recommendations are proposed:

1. **Strengthening evidence-based prescribing practices:** Pediatric antibiotic therapy should strictly follow internationally recognized clinical guidelines and national protocols, with antibiotics prescribed only when bacterial etiology is highly probable or microbiologically confirmed. Viral infections should not be treated with systemic antibiotics, and clinical decision-making must be based on validated diagnostic criteria.

2. **Prioritization of narrow-spectrum agents:** Whenever clinically justified, narrow-spectrum antibiotics should be preferred over broad-spectrum regimens. This approach minimizes selective pressure on commensal flora and reduces the risk of resistance development, while maintaining adequate therapeutic efficacy.

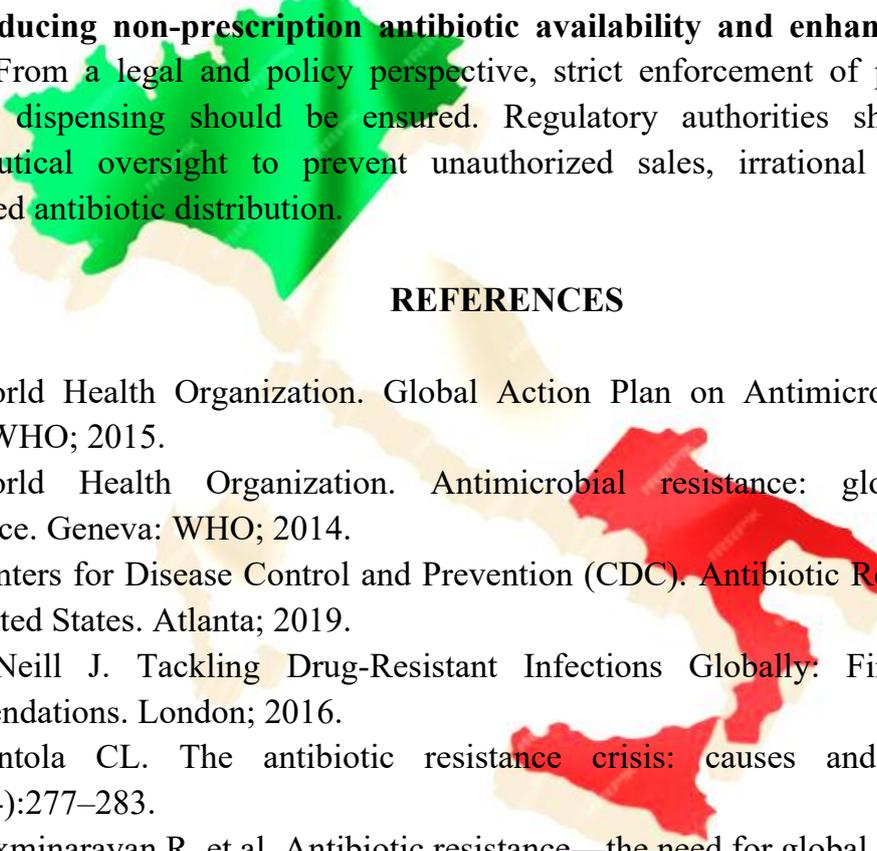
3. **Mandatory dose optimization and pharmacological accuracy:** Antibiotic dosing in children must be individualized based on age, body weight, renal and hepatic function, and disease severity. Incorrect dosing—especially subtherapeutic dosing—should be considered a significant risk factor for resistance selection and treatment failure. The pharmacokinetic and pharmacodynamic principles (PK/PD) should be integrated into routine pediatric prescribing.



4. **Implementation of antimicrobial stewardship programs (ASP):** Healthcare institutions should establish structured antimicrobial stewardship programs, including prescription audits, feedback mechanisms, clinical consultations with infectious disease specialists, and monitoring of antibiotic consumption indicators. Such programs are essential for improving antibiotic use quality and reducing unnecessary antimicrobial exposure.

5. **Expanding access to microbiological diagnostics:** Laboratory infrastructure should be strengthened to ensure timely pathogen identification and antimicrobial susceptibility testing. Even in outpatient settings, targeted microbiological testing should be encouraged in recurrent, severe, or treatment-resistant infections. Rapid diagnostic methods and point-of-care testing should be integrated into pediatric clinical workflows.

6. **Reducing non-prescription antibiotic availability and enhancing regulatory control:** From a legal and policy perspective, strict enforcement of prescription-only antibiotic dispensing should be ensured. Regulatory authorities should strengthen pharmaceutical oversight to prevent unauthorized sales, irrational marketing, and unregulated antibiotic distribution.



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