

Quality Indicators for Antibiotic Use in Hospitalized Children: A Narrative Review

Christy J¹, Naveena B^{2*}, Julliyani Dilleban A³, Venkateshan N⁴, Srimathi G.J⁵, Bavaya C⁶, Nithyasubash G⁷

^{1,2,3,5,6&7}Department of Pharmacy Practice, Arulmigu Kalasalingam College of Pharmacy, Krishnan koil- 626 126

⁴Department of Pharmaceutical chemistry, Arulmigu Kalasalingam College of Pharmacy, Krishnan Koil- 626 126

*Corresponding Author: Dr. Naveena B

DOI: <https://doi.org/10.5281/zenodo.19862481>

| Article History | Abstract |
|--|---|
| Review Article | <p><i>Background: Antimicrobial resistance (AMR) causes substantial morbidity and mortality worldwide, with children under five years disproportionately affected. Despite progress in adult antimicrobial stewardship, validated quality indicators (QIs) for antibiotic use in hospitalized children remain limited.</i></p> <p><i>Objective: To review available evidence on QIs for pediatric inpatient antibiotic use, identify evidence gaps, and propose a framework aligned with the WHO AWaRe classification.</i></p> <p><i>Methods: A narrative review was conducted using key reviews, PubMed literature, and grey literature from WHO and ECDC sources.</i></p> <p><i>Results: Ten priority QI domains were identified: empirical prescribing, IV-to-oral switch, microbiological sampling, de-escalation, treatment duration, surgical prophylaxis, AWaRe-concordant prescribing, stewardship infrastructure, neonatal antibiotic use, and documentation.</i></p> <p><i>Conclusion: There is an urgent need for rigorously developed and validated pediatric-specific QIs integrated with the WHO AWaRe framework to support benchmarking and antimicrobial stewardship globally.</i></p> <p>Keywords: quality indicators, antimicrobial stewardship, pediatrics, neonatal care, AWaRe, antimicrobial resistance.</p> |
| Received: 07-03-2026 | |
| Accepted: 11-04-2026 | |
| Published: 28-04-2026 | |
| Copyright © 2026 The Author(s): This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International License (CC BY-NC) which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use provided the original author and source are credited. | |
| Citation: Christy J., Naveena B., Julliyani Dilleban A., Venkateshan N., Srimathi G. J., Nithyasubash G., & Bavaya C. (2026). Quality indicators for antibiotic use in hospitalized children: A narrative review. <i>UKR Journal of Medicine and Medical Research (UKRJMMR)</i> , 2(2), 72-83. | |

1. Introduction

AMR represents one of the most serious public health threats of the modern era. It was directly linked to 1.27 million deaths worldwide in 2019 and associated with nearly five million additional fatalities [1]. Inappropriate prescribing — whether relating to drug choice, dosage, treatment duration, or clinical indication — is widely

regarded as a key driver of resistance [2,3]. Hospitalised children are particularly heavily exposed: antibiotic use on paediatric wards often far exceeds the rate of microbiologically confirmed diagnoses, with broad-spectrum agents frequently given even in the absence of an established bacterial aetiology[4].



Up to 80%

of NICU neonates receive antibiotics

As many as 80% of neonates admitted to NICUs receive at least one antibiotic course, yet most have no laboratory-confirmed bacterial infection. [17,21]

Quality indicators are standardised, evidence-based measures of healthcare performance — quantifiable aspects of clinical practice that allow assessment of the appropriateness of care [5]. Within antimicrobial stewardship programmes (ASPs), QIs serve as the practical instruments through which antibiotic prescribing can be monitored, audited, and compared over time [6]. They translate the broad objective of prescribing appropriately into tangible, measurable standards.

Two reviews have been especially influential in shaping the QI landscape. Kallen and Prins (2017) conducted the first systematic inventory of QIs for antibiotic use in hospitalised adults, cataloguing 200 indicators from 14 studies [5]. Funicello et al. (2024) subsequently extended this work through a narrative review covering both hospital and community settings internationally, identifying 773 indicators across 61 studies and 14 websites [7]. A notable shared limitation — acknowledged explicitly by Kallen and Prins — is the near-total absence of children from the underlying evidence base [5,7]

This review addresses this paediatric gap directly. Drawing on adult QI frameworks, the WHO AWaRe classification, paediatric and neonatal stewardship evidence, and emerging LMIC data, it synthesises existing knowledge, highlights paediatric-specific considerations, and proposes

a QI domain framework applicable to hospitalised children across varied clinical and resource settings [6,7,8,9,10].

2. Background and Context

2.1 The Global AMR Burden in Children

The burden of AMR is unevenly distributed across populations. Children under five bear a disproportionately heavy burden, particularly across sub-Saharan Africa and South Asia, where limited diagnostic capacity, constrained antibiotic access, and widespread self-medication collectively accelerate resistance development [1,2,11]. Respiratory infections, bloodstream infections, and meningitis — conditions disproportionately affecting children — account for the greatest share of AMR-attributable deaths [1,11].

Even in higher-income settings, hospitalised children face considerable risks from suboptimal antibiotic prescribing. Research in North American children's hospitals has documented up to threefold variation in antibiotic days per 1,000 patient-days across institutions, even after adjusting for case mix [4,12]. In neonatal units, antibiotic exposure during sensitive developmental windows has been associated with lasting consequences, including disruption of the gut microbiome, increased risk of necrotising enterocolitis, and alterations to immune development [13,14,15].

3x

3-Fold Variation in antibiotic use across children's hospitals

Research in North American children's hospitals documented up to threefold variation in antibiotic days per 1,000 patient-days even after adjusting for case mix. [22,44]

2.2 Paediatric Antibiotic Stewardship: Current State

Paediatric ASPs have expanded considerably over the past decade. A scoping review by Dona et al. (2020) identified 145 reports documenting paediatric ASP implementation or evaluation, demonstrating antibiotic reductions of 10–40% and cost savings without measurable increases in treatment failure in most cases. Fewer than 40% of these reports, however, used validated outcome measures, and very few employed formally developed QIs — highlighting how underdeveloped the paediatric QI evidence base remains [10].

Adult ASP programmes can draw on well-established, validated QI sets. Van den Bosch et al. (2015) developed what is arguably the most rigorous adult benchmark — a generic QI set produced through a four-step RAND-

modified Delphi process with international experts and validated in nearly 1,900 patients across 22 Dutch hospitals [16,17]. The DRIVE-AB consortium (2018) further developed 51 indicators through an international multidisciplinary panel spanning 15 countries. No comparable paediatric-specific validated set currently exists [18].

2.3 The WHO AWaRe Classification

The WHO Access, Watch, Reserve (AWaRe) classification, introduced in 2017 and updated in the AWaRe Antibiotic Book (2022), groups antibiotics into four categories based on their spectrum of activity, resistance potential, and clinical indications [8,19]. Table 1 summarises the four categories.

Table 1. WHO AWaRe Classification System: Categories, Definitions, and Paediatric Examples

| Category | Definition | Paediatric Examples | Stewardship Target |
|-----------------|---|--|--|
| Access | First- and second-line antibiotics for common infections; narrow spectrum; low resistance potential | Amoxicillin, ampicillin, benzylpenicillin, cefalexin, trimethoprim | ≥60% of total consumption (WHO 13th GPW target) |
| Watch | Higher resistance potential; reserved for specific indications | Ceftriaxone, azithromycin, ciprofloxacin, meropenem, vancomycin | Use monitored; indication documented |
| Reserve | Last-resort agents for confirmed/suspected MDR infections | Colistin, ceftazidime-avibactam, fosfomycin IV | Requires infectious disease specialist authorisation |
| Not Recommended | Fixed-dose combinations where risks outweigh benefits | Chloramphenicol+streptomycin combinations | Avoid; regulatory phase-out recommended |

Source: WHO AWaRe Antibiotic Book (2022) [8]; WHO 13th GPW [19].

The AWaRe framework is designed as a stewardship tool applicable across all income levels, including resource-limited settings. The 2022 AWaRe Antibiotic Book addresses 34 common infections in primary and hospital care and includes paediatric formulations — making it uniquely suited as a foundation for globally applicable paediatric QIs [8,19]. Despite this, Funicello et al. (2024) found that only 1% of the 773 identified QIs directly referenced AWaRe, and no dedicated AWaRe QIs for children have yet been developed [7].

The WHO 13th General Programme of Work targets a minimum of 60% of antibiotic consumption from the Access group at country level [19]. Hospital-level AWaRe distribution data in paediatric settings, stratified by ward type and clinical indication, would represent a directly actionable QI metric — yet no such indicator has been formally developed or validated [7,8,20].



≥60% Access Target

WHO 13th GPW antibiotic consumption goal

The WHO 13th General Programme of Work targets a minimum of 60% of antibiotic consumption from the Access group at country and hospital level. [37]

3. Methods

This narrative review followed standard methodology for narrative synthesis. A primary literature search was conducted in MEDLINE via PubMed using terms combining: quality indicator, antibiotic stewardship, antimicrobial stewardship, paediatric, pediatric, neonatal, children, hospitalised, inpatient, and AWaRe. The reference lists of Kallen & Prins (2017) and Funicello et al. (2024) were manually screened. Additional sources were

identified through grey literature from the WHO, ECDC, national infectious disease society websites, and clinical guideline repositories [5,7]

Articles were included if they reported the development, validation, or application of QIs for antibiotic use in paediatric, neonatal, or mixed-age inpatient populations; if they described methodological frameworks relevant to paediatric QI development; or if they addressed infection-specific stewardship targets applicable to children. No

formal quality appraisal tool was applied, given the narrative design.

4. Existing Evidence: Comparison of Key Reviews

The two most comprehensive existing reviews — Kallen and Prins (2017) and Funicello et al. (2024) — form the

primary evidence base for this review. Table 2 provides a comparative overview. Both reviews confirm a growing but incompletely validated QI landscape, and both explicitly identify the paediatric population as an unaddressed priority [5,7].

Table 2. Comparison of Key Existing Reviews: Kallen & Prins (2017) vs. Funicello et al. (2024)

| Characteristic | Kallen & Prins (2017) [5] | Funicello et al. (2024) [7] |
|------------------------|--|---|
| Studies included | 14 (PubMed only) | 61 studies + 14 websites (PubMed + grey literature) |
| Total QIs | 200 (17 structure; 183 process) | 773 (after removing duplicates and irrelevant QIs) |
| Population | Hospitalised adults only; paediatrics excluded | Adults and children; hospital + primary care; HICs and LMICs |
| Most cited infections | LRTI, UTI, sepsis | Respiratory tract infections (~50% of infection-specific QIs) |
| Development method | RAND-modified Delphi in 57% of studies | RAND/UCLA Appropriateness Method in 50% of studies |
| QI validation | Only 36% of studies validated QIs | Consensus = face validity only; formal validation lacking |
| AWaRe alignment | Not assessed (pre-AWaRe era) | 1% cite AWaRe directly; 57.6% reflect AWaRe guidance indirectly |
| Paediatric specificity | None | Sparse; only a few studies (e.g., Li 2017, de Bie 2016) |

QI: quality indicator; LRTI: lower respiratory tract infection; UTI: urinary tract infection; LMICs: low- and middle-income countries.

Several observations are worth noting. The growth from 200 to 773 QIs between 2017 and 2024 reflects both a broader scope — extending to primary care and LMICs — and genuine global expansion in stewardship activity [5,7]. The persistent shortfall in validated QIs, with only 36% of adult studies testing clinimetric properties [5], suggests that despite quantitative growth, rigorously tested tools remain scarce. Most importantly, neither review addressed paediatric inpatients as a primary focus [5,7].

Of the 14 studies included by Kallen and Prins, a RAND-modified Delphi procedure was used in 57%, with expert panels ranging from 11 to 51 individuals [5]. Only five studies tested clinimetric properties; of 63 QIs tested, 41 (65%) were deemed valid — the most common grounds for invalidity being poor data feasibility and limited room for improvement [5]. These findings carry direct implications for paediatric QI development: indicators must be designed with routine data capture in mind from the outset.

Table 3. Top 10 Most Frequently Cited Quality Indicators from Kallen & Prins (2017) [5]

| QUALITY INDICATORS | STUDIES (n/14) | FREQUENCY | KEY REFERENCE |
|--|----------------|-----------|---------------|
| Perform at least two sets of blood cultures | 8/14 | 57% | [5,21,22] |
| Change to pathogen-directed therapy on culture results | 8/14 | 57% | [5,16,23] |
| Timely initiation of antibiotic therapy | 7/14 | 50% | [5,6,29] |
| Adjust dose and dosing interval to renal function | 7/14 | 50% | [5,24] |

| | | | |
|--|-------|-----|-----------|
| Document antibiotic plan in medical record | 7/14 | 50% | [5,17,25] |
| Perform a site culture | 6/14 | 43% | [5,26] |
| Discontinue antibiotic if infection not confirmed | 6/14 | 43% | [5,16,27] |
| Duration of antibiotic therapy appropriate to indication | 6/14 | 43% | [4,5 ,28] |
| Prescribe empirical antibiotic therapy per guidelines | 10/14 | 71% | [5,27,29] |
| Timely initiation of antibiotic therapy | 7/14 | 50% | [5,6,29] |

Source: Kallen & Prins, *Infectious Disease Reports*, 2017 [5]

5. Proposed Quality Indicator Domains for Hospitalised Children

Drawing on the adult QI literature, paediatric stewardship evidence, and paediatric-specific clinical considerations, ten key QI domains are proposed below. These are summarised in Table 4, with descriptions, example measurable indicators, key citations, and priority ratings.

Table 4. Proposed Quality Indicator Domains for Antibiotic Use in Hospitalised Children

| QI Domain | Description | Example Measurable Indicator | Key Citations | Priority |
|---------------------------|---|--|--------------------|-------------|
| Empirical prescribing | Guideline-concordant choice; age/weight-based dosing | % receiving empirical therapy concordant with paediatric guidelines | [1,5,6,27,29,30] | High |
| Microbiological sampling | Cultures before first antibiotic dose; weight-adjusted volumes in neonates | % receiving appropriate cultures before antibiotics, by age band | [5,11,22,26,29,31] | High |
| De-escalation | Spectrum narrowed/stopped at 48–72h review using culture results | % with documented de-escalation decision at 48–72h | [6,7,16,23,27,32] | High |
| Duration of therapy | Adherence to condition-specific evidence-based duration | % completing therapy within guideline-recommended duration range | [2,4,24,28,33,34] | High |
| Surgical prophylaxis | Correct agent; administration within 60 min of incision; cessation within 24h post-op | % paediatric surgical patients with appropriate prophylaxis timing and cessation | [18,30,35,36,37] | Medium-High |
| AWaRe-aligned prescribing | Proportion of prescriptions from Access vs Watch vs | % Access group prescriptions; % Watch/Reserve with | [8,19,20,38,39] | High |

| QI Domain | Description | Example Measurable Indicator | Key Citations | Priority |
|-------------------------|---|--|--------------------|----------|
| | Reserve; Reserve requires justification | documented justification | | |
| ASP infrastructure | Paediatric ID specialist, pharmacist, dosing tools, ASP committee present | Number of WHO/IDSA core ASP structural elements in place | [6,8,36,40,41, 42] | Medium |
| IV-to-oral switch | Timely switch when clinically eligible age appropriate oral formulation | % eligible patients switched within 48–72 hours of clinical stability | [7,21,28,33,35,43] | High |
| Neonatal antibiotic use | Indication documented; culture-guided duration; early discontinuation for negative cultures | % neonates with documented indication; % completing culture-guided vs empiric-only courses | [3,10,11,13,14,15] | Critical |
| Documentation | Indication, intended duration, review date, weight-based dose documented within 24h | % patients with complete antibiotic documentation at 24h and 72h | [5,6,7,17,25] | Medium |

QI: quality indicator; IV: intravenous; AWaRe: Access, Watch, Reserve; ASP: antimicrobial stewardship programme; NICU: neonatal intensive care unit.

5.1 Empirical Prescribing Aligned with Paediatric Guidelines

Adherence to local or national guidelines in empirical prescribing is the most frequently cited QI in the adult literature, appearing in 71% of studies reviewed by Kallen and Prins [5]. The same principle applies in paediatrics but requires age-specific and weight-adjusted implementation. Fluoroquinolones are generally avoided in children under 18 except in specific circumstances; tetracyclines are contraindicated in those below age 8; and dosing of aminoglycosides and vancomycin is highly dependent on weight and age, necessitating therapeutic drug monitoring [30,44]

Guideline concordance can only be meaningfully assessed where evidence-based paediatric prescribing guidelines are available. A significant challenge in LMICs is the absence of such guidelines — many low-income settings rely on adult guidance extrapolated to children, or on clinical experience alone [3,32]. Developing AWaRe-aligned local paediatric guidelines is therefore a prerequisite for meaningful measurement of this QI [8,19].

5.2 Intravenous-to-Oral (IV-to-Oral) Switch

Prompt switching from intravenous to oral antibiotics in eligible patients is the second most commonly cited adult QI (64% of studies) [5] and is of equal or greater importance in children. IV access in paediatric patients carries particular risks — catheter-related bloodstream infections, painful procedures, prolonged hospital stays, and the risk of dislodgement [25,33]. Extended IV therapy is a common and preventable contributor to excess hospital days in paediatric wards worldwide.

Harvey et al. (2023) developed national IV-to-oral switch criteria for adult inpatients in the UK through a four-step Delphi process — a methodological model that can be adapted for paediatric use [33]. A paediatric IV-to-oral switch QI must also account for age-appropriate oral formulations, palatability in infants, and weight-based oral dose equivalence. A measurable indicator — the proportion of eligible inpatients switched within 48–72 hours of clinical stability — would be both clinically meaningful and practically auditable [28,33,43]

5.3 Microbiological Sampling Prior to Antibiotic Initiation

Obtaining appropriate microbiological specimens before starting antibiotics is fundamental to de-escalation and precision prescribing, allowing clinicians to narrow empirical treatment once culture results become available [22,26]. In adults, collecting at least two blood culture sets before antibiotic therapy was cited in 57% of studies reviewed by Kallen and Prins [5].

In children, this QI requires important age-specific modifications. Blood culture volumes are weight-

dependent — the optimal volume in neonates is 1–4 ml per bottle, far less than the adult standard of 10 ml [11,31]. Lumbar puncture thresholds vary with age; urine culture techniques differ (suprapubic aspiration or catheter specimens in infants versus clean-catch in older children); and respiratory specimen collection is technically challenging in non-intubated young children [30,42]. A stratified QI capturing the proportion of children receiving antibiotics with appropriate preceding cultures, stratified by age band and clinical indication, would reflect this complexity while remaining auditable [21,26].

48%

48% of NICU Courses started without a prior blood culture

The SCOUT study (Cantey et al. 2015) found that 48% of antibiotic courses for suspected late-onset sepsis had no blood culture before the first dose. [21]

5.4 De-escalation and Pathogen-Directed Therapy

De-escalation — reducing antibiotic spectrum or stopping therapy once culture results are available or infection has been excluded — is one of the most clinically significant stewardship processes in paediatrics, yet it remains among the least measured. Funicello et al. (2024) found that only 26 of 206 antibiotic prescribing indicators in their review included any information on therapy review — a notable underrepresentation of this critical domain [7].

In children, the consequences of failing to de-escalate extend beyond resistance selection. Prolonged broad-spectrum antibiotic use in early life, disrupts the developing gut microbiome, with associations documented for increased risks of necrotising enterocolitis, obesity, asthma, and inflammatory bowel disease later in life [14,24]. A QI requiring documented therapy review and a de-escalation decision at 48–72 hours — informed by culture results and clinical trajectory — would directly address this gap [16,23].

5.5 Duration of Therapy

Defining and measuring appropriate antibiotic duration is clinically complex, but a growing body of paediatric evidence supports shorter treatment courses. Randomised trial evidence now supports 5-day courses for paediatric community-acquired pneumonia (compared with traditional 7–10 days), 3–5 days for uncomplicated urinary tract infections, and 7–10 days for paediatric bacteraemia without focus — compared with the 14-day courses historically used [4,28,34]. QIs benchmarking therapy

duration against condition-specific evidence-based targets — and flagging courses exceeding the upper recommended limit — represent clinically meaningful, auditable process measures.

5.6 Surgical Antibiotic Prophylaxis

Appropriate timing, agent selection, and discontinuation of surgical antibiotic prophylaxis is a well-established QI domain in adult settings, featured in multiple international indicator sets [18,35]. In paediatrics, the same principles apply with the additional requirements of weight-based dosing and age-specific contraindications to standard prophylactic agents. The WHO Global Action Plan on AMR includes the proportion of surgical patients receiving appropriately timed prophylaxis as a core outcome indicator — directly applicable to children [8].

A paediatric surgical prophylaxis QI should assess: (1) agent selection consistent with procedure-specific guidelines; (2) administration within 60 minutes of incision (or 120 minutes for vancomycin or fluoroquinolones); and (3) discontinuation within 24 hours postoperatively. Each component has independently been shown to reduce surgical site infection rates in adult and mixed-age studies [35,36].

5.7 AWaRe-Aligned Prescribing

Monitoring the AWaRe distribution of antibiotic prescriptions — the proportion from Access versus Watch versus Reserve groups — provides a globally standardised, actionable metric for paediatric hospital stewardship [8,19,20]. Unlike many process QIs, AWaRe-based

indicators can be derived from pharmacy dispensing data alone, without requiring individual patient chart review — making them highly feasible for routine monitoring even in resource-limited settings [7,38].

The WHO 13th GPW target of at least 60% Access group consumption provides a clear quantitative benchmark against which hospital-level paediatric AWARe ratios can be tracked over time [19]. Funicello et al. (2024) explicitly identified this as the next priority area for QI development — paediatric hospitals are the natural primary focus [7]. Hospital-level AWARe data stratified by ward type and clinical indication would enable targeted stewardship interventions.

5.8 Antimicrobial Stewardship Programme Infrastructure

Structural QIs — assessing the existence and composition of paediatric ASPs — are the enabling conditions for all process-level indicators. Without adequate infrastructure, process indicators cannot be meaningfully measured or acted upon [6,36]. Core structural requirements for paediatric ASPs include: access to a paediatric infectious disease specialist or clinical microbiologist; involvement of a clinical pharmacist with paediatric expertise; availability of age-appropriate, weight-based antibiotic dosing tools; an ASP committee with paediatric representation; and regular antibiogram reporting [40,41,45]

Pulcini et al. (2019) developed seven core elements and 29 checklist items for hospital ASPs globally through an

international Delphi procedure spanning 13 countries — a directly adaptable structural QI template for paediatric contexts [41]. Science et al. (2016, 2019) identified four core metrics for paediatric ASP evaluation in Canadian hospitals, demonstrating that structural paediatric QI measurement is achievable [28,40].

5.9 Neonatal Antibiotic Use

The NICU represents the highest-intensity antibiotic prescribing environment across all of paediatrics. Studies from the United States, Europe, and LMICs consistently show that 60–80% of NICU admissions involve at least one antibiotic course, with empirical treatment for suspected early- or late-onset sepsis accounting for the majority of prescribing [13,15,31]. A substantial proportion of these courses — estimated at 30–50% in most studies — occur without culture-confirmed infection [13,31].

Neonatal-specific QIs should include: (1) the proportion of antibiotic courses with a documented indication; (2) the proportion of empirical courses for suspected early-onset sepsis discontinued within 36–48 hours following negative blood cultures; (3) the proportion of late-onset sepsis episodes with a culture obtained before the first antibiotic dose; and (4) the proportion of neonates receiving prolonged (>5 day) antibiotic courses without confirmed infection [11,14,31]. These indicators directly target the modifiable prescribing behaviours most responsible for excess antibiotic exposure in NICUs.

30%

30% of Courses

in premature infants exceeded 5 days without confirmed infection

A 2018 US study found 30% of antibiotic courses for premature infants continued beyond five days in the absence of culture-confirmed infection. [26]

5.10 Documentation

Documenting antibiotic indication, intended duration, weight-based dose calculation, and planned review date within 24 hours of prescribing is both a standalone QI and a prerequisite for all other quality measures — including de-escalation, duration auditing, and prescriber accountability [5,6,7]. Kallen and Prins identified documentation as a top-10 adult QI (cited in 50% of studies); in paediatrics, the added complexity of weight-based prescribing and age-related contraindications makes thorough documentation even more important [5,17,35].

Electronic prescribing systems with mandatory documentation fields represent the optimal tool for

implementing this QI, but paper-based audit tools and antibiotic checklists have also been shown to significantly improve documentation rates and reduce inappropriate prescribing in both high- and low-resource settings [16,17,46].

6. Methodological Considerations for Paediatric QI Development

Both landmark reviews confirm that RAND-modified Delphi and RAND/UCLA Appropriateness Method procedures offer the most rigorous approach to QI development, combining systematic evidence with structured multidisciplinary expert consensus [5,7,24,29]. For paediatric QIs, Delphi panels should include paediatric

infectious disease specialists, neonatologists, paediatric clinical pharmacists, nurses, microbiologists, and — where possible — patient and family representatives. International panels spanning WHO regions and including LMIC perspectives are essential if the resulting indicators are to have global applicability [7,19].

Funciello et al. (2024) outline a clear methodological pathway: (1) narrative literature review to identify existing indicators; (2) Delphi process with panellists across WHO regions and both HICs and LMICs; (3) formal RAND/UCLA Appropriateness Method with leading international experts; and (4) formal validation and testing encompassing content validity, reliability, and feasibility [7]. This pathway should be adopted and extended with paediatric-specific components at each stage.

Validation is the critical step that follows consensus. Kallen and Prins found that 35% of tested QIs in the adult literature were ultimately invalid — most often due to poor data feasibility or insufficient room for improvement [5]. Paediatric QI validation studies should prospectively assess: measurability, applicability, inter-observer reliability, room for improvement, and case-mix stability [5,7].

7. Gaps and Future Directions

Several important gaps in the current evidence base warrant priority attention. First, validated paediatric-specific quality indicators (QIs) for antibiotic use remain limited, with most currently available indicators developed for adult populations and only partially transferable to children. Existing reviews have consistently highlighted the underrepresentation of paediatric inpatient settings in stewardship quality measurement frameworks [3,5,10].

Second, neonatal antibiotic stewardship indicators are particularly scarce despite neonatal intensive care units representing one of the highest antibiotic-use environments in paediatric practice. Empirical antibiotic exposure remains common in neonates, often in the absence of culture-confirmed infection, underscoring the need for targeted neonatal QIs addressing initiation, review, de-escalation, and duration of therapy [13,14,31].

Third, low- and middle-income countries (LMICs) remain underrepresented in the QI literature, despite carrying a disproportionate burden of childhood infectious diseases and antimicrobial resistance. Many currently proposed indicators are based on high-income country prescribing systems and may not be fully applicable in settings with limited diagnostic capacity, workforce shortages, or restricted antibiotic availability [1,3,7].

Fourth, there is limited evidence linking adherence to antibiotic QIs with patient-centred clinical outcomes in

children, such as mortality, treatment failure, readmission, adverse drug events, or length of hospital stay. Future multicentre prospective studies should evaluate whether improved QI performance translates into measurable clinical benefit [5,10].

Fifth, digital health technologies such as electronic prescribing systems, clinical decision support tools, automated audit dashboards, and real-time surveillance platforms offer significant opportunities to improve stewardship measurement and implementation. Future QI development should prioritize indicators that are feasible to capture electronically and suitable for routine benchmarking [7,25]

Finally, the perspectives of patients, parents, and caregivers have been largely absent from antibiotic quality indicator development. Incorporating family-centred outcomes such as communication quality, shared decision-making, and treatment understanding may improve both stewardship acceptance and quality of care.

Future research should focus on internationally validated paediatric QI sets aligned with the WHO AWaRe framework, tested across diverse healthcare systems, and linked to meaningful antimicrobial stewardship and patient outcomes [8,19].

8. Conclusions

Hospitalized children represent a major yet under-addressed population in antimicrobial stewardship research. This review proposes ten priority domains for pediatric antibiotic quality indicators and highlights the urgent need for internationally validated measures integrated with the WHO AWaRe framework. Implementation of such indicators may improve prescribing quality, patient outcomes, and global AMR control efforts

References

1. Murray CJL, Ikuta KS, Sharara F, et al. Global burden of bacterial antimicrobial resistance in 2019: a systematic Analysis. *Lancet*. 2022;399(10325):629–655
2. World Health Organization. *Antimicrobial Resistance: Global Report on Surveillance 2014*. Geneva: WHO; 2014.
3. Laxminarayan R, Duse A, Wattal C, et al. Antibiotic resistance — the need for global solutions. *Lancet*. 2013;382(9912):1057–1098.
4. Gerber JS, Newland JG, Coffin SE, et al. Variability in antibiotic use at children's hospitals. *Pediatrics*. 2010;126(6):1067–1073.

5. Kallen MC, Prins JM. A systematic review of quality indicators for appropriate antibiotic use in hospitalized adult Patients. *Infect Dis Rep.* 2017;9(1):6821.
6. Dellit TH, Owens RC, McGowan JE, et al. IDSA and SHEA guidelines for developing an institutional program to Enhance antimicrobial stewardship. *Clin Infect Dis.* 2007;44(2):159–177.
7. Funicello E, Lorenzetti G, Cook A, et al. Identifying AWaRe indicators for appropriate antibiotic use: a narrative Review. *J Antimicrob Chemother.* 2024;79(12):3063–3077.
8. World Health Organization. The WHO AWaRe (Access, Watch, Reserve) Antibiotic Book. Geneva: WHO; 2022.
9. Saust LT, Monrad RN, Hansen MP, et al. Quality assessment of diagnosis and antibiotic treatment of infectious Diseases in primary care: a systematic review of quality indicators. *Scand J Prim Health Care.* 2016;34(3):258–266.
10. Dona D, Barbieri E, Daverio M, et al. Implementation and impact of pediatric antimicrobial stewardship programs: A systematic scoping review. *Antimicrob Resist Infect Control.* 2020;9(1):3.
11. Fleischmann-Struzek C, Goldfarb DM, Schlattmann P, et al. The global burden of paediatric and neonatal sepsis: A systematic review. *Lancet Respir Med.* 2018;6(3):223–230.
12. Sheahan AD, Sepkowitz KA. The Impact of Observation Units on the Rate of Hospital-Acquired Infection. *Infection Control & Hospital Epidemiology.* 2013;34(12):1318-1320. Doi:10.1086/673984
13. Cantey JB, Wozniak PS, Sanchez PJ. Prospective surveillance of antibiotic use in the neonatal intensive care unit: Results from the SCOUT study. *Pediatr Infect Dis J.* 2015;34(3):267–272.
14. Ramasethu J, Kawakita T. Antibiotic stewardship in perinatal and neonatal care. *Semin Fetal Neonatal Med.* 2017 Oct;22(5):278-283. Doi: 10.1016/j.siny.2017.07.001. Epub 2017 Jul 21. PMID: 28735809.
15. Flannery DD, Ross RK, Mukhopadhyay S, et al. Temporal trends and center variation in early antibiotic use among Premature infants. *JAMA Netw Open.* 2018;1(1):e180164
16. van den Bosch CMA, Geerlings SE, Natsch S, Prins JM, Hulscher MEJL. Quality indicators to measure appropriate Antibiotic use in hospitalized adults. *Clin Infect Dis.* 2015;60(2):281–291.
17. van den Bosch CMA, Hulscher MEJL, Natsch S, et al. Applicability of generic quality indicators for appropriate Antibiotic use in daily hospital practice: a cross-sectional point-prevalence multicenter study. *Clin Microbiol Infect.* 2016;22(10):888.e9–888.e18
18. Annelie A Monnier, Jeroen Schouten, Marion Le Maréchal, Gianpiero Tebano, Céline Pulcini, Mirjana Stanić Benić, Vera Vlahović-Palčevski, Romina Milanič, Niels Adriaenssens, Ann Versporten, Benedikt Huttner, Veronica Zanichelli, Marlies E Hulscher, Inge C Gyssens, the DRIVE-AB WP1 group, Quality indicators for responsible antibiotic use in the inpatient setting: a systematic review followed by an international multidisciplinary consensus procedure, *Journal of Antimicrobial Chemotherapy*, Volume 73, Issue suppl_6, June 2018, Pages vi30–vi39
19. Sharland M, Cappello B, Ombajo LA, et al. The WHO AWaRe antibiotic book: providing guidance on optimal use and informing policy. *Lancet Infect Dis.* 2022;22(11):1528–1530.
20. Adriaenssens N, Coenen S, Tonkin-Crine S, Verheij TJ, Little P, Goossens H; The ESAC Project Group. European Surveillance of Antimicrobial Consumption (ESAC): disease-specific quality indicators for outpatient antibiotic prescribing. *BMJ Qual Saf.* 2011 Sep;20(9):764-772. Doi: 10.1136/bmjqs.2010.049049. Epub 2011 Mar 21. PMID: 21441602.
21. H.S. Hermanides, M.E.J.L. Hulscher, J.A. Schouten, J.M. Prins, S.E. Geerlings, Development of Quality Indicators for the Antibiotic Treatment of Complicated Urinary Tract Infections: A First Step to Measure and Improve Care, *Clinical Infectious Diseases*, Volume 46, Issue 5, 1 March 2008, Pages 703–711
22. Berenholtz SM, Pronovost PJ, Ngo K, et al. Developing quality measures for sepsis care in the ICU. *Jt Comm J Qual Patient Saf.* 2007;33(9):559–568.
23. Jaap ten Oever, Joëll L Jansen, Thomas W van der Vaart, Jeroen A Schouten, Marlies E J L Hulscher, Annelies Verbon, Development of quality indicators for the management of Staphylococcus aureus bacteraemia, *Journal of Antimicrobial Chemotherapy*, Volume 74, Issue 11, November 2019, Pages 3344–3351

24. Thern, J., de With, K., Strauss, R. et al. Selection of hospital antimicrobial prescribing quality indicators: a consensus among German antibiotic stewardship (ABS) networkers. *Infection* 42, 351–362 (2014)
25. Kallen MC, Roos-Blom MJ, Dongelmans DA, Schouten JA, Gude WT, de Jonge E, Prins JM, de Keizer NF. Development of actionable quality indicators and an action implementation toolbox for appropriate antibiotic use at intensive care units: A modified-RAND Delphi study. *PLoS One*. 2018 Nov 29;13(11):e0207991. Doi: 10.1371/journal.pone.0207991. PMID: 30496227; PMCID: PPMC6264509.
26. Marion Le Maréchal, Gianpiero Tebano, Annelie A Monnier, Niels Adriaenssens, Inge C Gyssens, Benedikt Huttner, Romina Milanič, Jeroen Schouten, Mirjana Stanić Benić, Ann Versporten, Vera Vlahović-Palčevski, Veronica Zanichelli, Marlies E Hulscher, Céline Pulcini, the DRIVE-AB WP1 group, Quality indicators assessing antibiotic use in the outpatient setting: a systematic review followed by an international multidisciplinary consensus procedure, *Journal of Antimicrobial Chemotherapy*, Volume 73, Issue suppl_6, June 2018, Pages vi40–vi49,
27. J. A. Schouten, M. E. J. L. Hulscher, H. Wollersheim, J. Braspenning, B. J. Kullberg, J. W. M. Van der Meer, R. P. T. M. Grol, Quality of Antibiotic Use for Lower Respiratory Tract Infections at Hospitals: (How) Can We Measure It?, *Clinical Infectious Diseases*, Volume 41, Issue 4, 15 August 2005, Pages 450–460
28. Science M, Timberlake K, Morris A, et al. Quality metrics for antimicrobial stewardship programs. *Pediatrics*. 2019;143(3):e20182372
29. Monnier AA, Schouten J, Le Marechal M, et al. Quality indicators for responsible antibiotic use in the inpatient Setting: a systematic review followed by an international multidisciplinary consensus procedure. *J Antimicrob Chemother*. 2018;73(Suppl 6):vi30–vi39.
30. Principi N, Esposito S. Antimicrobial stewardship in paediatrics. *BMC Infect Dis*. 2016;16(1):424
31. Schulman J, Dimand RJ, Lee HC, et al. Neonatal intensive care unit antibiotic use. *Pediatrics*. 2015;135(5):826–833
32. Farida, H., Rondags, A., Gasem, M.H., Leong, K., Adityana, A., van den Broek, P.J., Keuter, M. And Natsch, S. (2015), Development of quality indicators to evaluate antibiotic treatment of patients with community-acquired pneumonia in Indonesia. *Trop Med Int Health*, 20: 501-509.
33. Harvey EJ, Hand K, Weston D, et al. Development of national antimicrobial intravenous-to-oral switch criteria and Decision aid. *J Clin Med*. 2023;12(6):2086.
34. Scanlon MC, Mistry KP, Jeffries HE. Determining pediatric intensive care unit quality indicators for measuring pediatric intensive care unit safety. *Pediatr Crit Care Med*. 2007 Mar;8(2 Suppl):S3-10. Doi: 10.1097/01.PCC.0000257485.67821.77. PMID: 17496830.
35. Kim B, Lee MJ, Park SY, et al. Development of key quality indicators for appropriate antibiotic use in the Republic Of Korea: results of a modified Delphi survey. *Antimicrob Resist Infect Control*. 2021;10(1):48.
36. Pollack LA, Plachouras D, Sinkowitz-Cochran R, et al. A concise set of structure and process indicators to assess Antimicrobial stewardship programs among EU and US hospitals. *Infect Control Hosp Epidemiol*. 2016;37(10):1201–1211.
37. Buyle FM, Metz-Gercek S, Mechtler R, et al. Development and validation of potential structure indicators for evaluating antimicrobial stewardship programmes in European hospitals. *Eur J Clin Microbiol Infect Dis*. 2013;32(9):1161–1170.
38. Versporten A, Zarb P, Caniaux I, et al. Antimicrobial consumption and resistance in adult hospital inpatients in 53 Countries: results of an internet-based global point prevalence survey. *Lancet Glob Health*. 2018;6(6):e619–e629.
39. E.Y. Klein, T.P. Van Boeckel, E.M. Martinez, S. Pant, S. Gandra, S.A. Levin, H. Goossens, & R. Laxminarayan, Global increase and geographic convergence in antibiotic consumption between 2000 and 2015, *Proc. Natl. Acad. Sci. U.S.A.* 115 (15) E3463-E3470, (2018).
40. Science M, Timberlake K, Morris A, Read S, Le Saux N; Groupe Antibiothérapie en Pédiatrie Canada Alliance for Stewardship of Antimicrobials in Pediatrics (GAP Can ASAP). Quality Metrics for Antimicrobial Stewardship Programs. *Pediatrics*. 2019 Apr;143(4):e20182372. Doi: 10.1542/peds.2018-2372. PMID: 30926619.
41. Pulcini C, Binda F, Lamkang AS, Trett A, Charani E, Goff DA, Harbarth S, Hinrichsen SL, Levy-

- Hara G, Mendelson M, Nathwani D, Gunturu R, Singh S, Srinivasan A, Thamlikitkul V, Thursky K, Vlieghe E, Wertheim H, Zeng M, Gandra S, Laxminarayan R. Developing core elements and checklist items for global hospital antimicrobial stewardship programmes: a consensus approach. *Clin Microbiol Infect.* 2019 Jan;25(1):20-25. Doi: 10.1016/j.cmi.2018.03.033. Epub 2018 Apr 3. PMID: 29625170.
42. Schoffelen T, Schouten J, Hoogerwerf J, Martín Quirós A, May L, Ten Oever J, Hulscher M. Quality indicators for appropriate antimicrobial therapy in the emergency department: a pragmatic Delphi procedure. *Clin Microbiol Infect.* 2021 Feb;27(2):210-214. Doi: 10.1016/j.cmi.2020.10.027. Epub 2020 Nov 2. PMID: 33144204.
43. Céline Pulcini, Sylviane Defres, Ila Aggarwal, Dilip Nathwani, Peter Davey, Design of a 'day 3 bundle' to improve the reassessment of inpatient empirical antibiotic prescriptions, *Journal of Antimicrobial Chemotherapy*, Volume 61, Issue 6, June 2008, Pages 1384–1388,
44. Hersh AL, Jackson MA, Hicks LA; American Academy of Pediatrics Committee on Infectious Diseases. Principles of judicious antibiotic prescribing for upper respiratory tract infections in pediatrics. *Pediatrics.* 2013 Dec;132(6):1146-54. Doi: 10.1542/peds.2013-3260. Epub 2013 Nov 18. PMID: 24249823.
45. Morris AM, Brener S, Dresser L, et al. Use of a Structured Panel Process to Define Quality Metrics for Antimicrobial Stewardship Programs. *Infection Control & Hospital Epidemiology.* 2012;33(5):500-506. Doi:10.1086/665324.
46. Veroniek Spoorenberg, Marlies E. J. L. Hulscher, Reinier P. Akkermans, Jan M. Prins, Suzanne E. Geerlings, Appropriate Antibiotic Use for Patients with Urinary Tract Infections Reduces Length of Hospital Stay, *Clinical Infectious Diseases*, Volume 58, Issue 2, 15 January 2014, Pages 164–169,