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Impact of Repeated Point Prevalence Surveys on Pediatric Antimicrobial Prescribing during the TeleKasper Study

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Key Words: Pediatric, Antibiotic Stewardship, repeated Point Prevalence Survey, Antimicrobial Prescription, Telemedicine

Abstract

Purpose

Antimicrobial prescribing in hospitalized children is frequently inappropriate. Point prevalence surveys (PPS) are used to assess prescribing quality, but their potential impact on prescribing behavior has not been well studied. We performed repeated PPS during a multimodal antimicrobial stewardship intervention in pediatric inpatients.

Methods

We analyzed data from the prospective stepped-wedge cluster-randomized TeleKasper trial including 33 non-university pediatric hospitals in Germany. Quarterly PPS were conducted between March 2022 and June 2024. Prescribing quality was assessed by pediatric infectious disease specialists. *Optimal care* was defined as appropriate treatment indication, antibiotic selection, and dosing. Effects of intervention and repeated PPS on *optimal care* were analyzed using mixed-effects logistic regression.

Results

Among 868 children receiving antibiotic treatment, no independent improvement in *optimal care* was observed after introduction of the TeleKasper intervention. In contrast, each additional PPS (also during the control phase) was associated with a 14% increase in the odds of *optimal care* (OR 1.14, 95% CI 1.07–1.20). The proportion of patients receiving *optimal care* increased from 25.8% in the first two PPS to 53.0% in the final two surveys. Appropriate treatment duration improved from 22.7% to 39.2%, while cephalosporin use decreased from 31.4% to 17.4%.

Conclusions

Repeated PPS were associated with improvements in quality of antimicrobial prescribing independent of the multimodal stewardship intervention. Beyond their role as surveillance tools, repeated PPS may themselves contribute to improving antimicrobial stewardship in pediatric hospitals.

Introduction

Antimicrobial resistance (AMR) represents a major global health threat [1]. Infectious diseases remain a leading cause of pediatric hospitalization and account for frequent use of antibiotic treatment (ABT). Inappropriate antibiotic use promotes the emergence of antimicrobial resistance and is associated with avoidable adverse drug events and increased healthcare costs [2-5]. The heterogeneity of the pediatric population (premature infants to young adults) increases the risk of medication errors [6]. Inappropriate antibiotic prescribing occurs across all pediatric subspecialties, highlighting substantial potential for improvement [7-11]. Effective antimicrobial stewardship programs (ASP) require multidisciplinary expertise, including pediatric infectious disease specialists, pharmacists, and microbiologists. However, such expertise is often unavailable in non-university pediatric hospitals, in Germany [12].

To improve prescribing quality, the “Telemedicine Competence Network Antibiotic Stewardship in Pediatrics” (TeleKasper) trial implemented a multimodal antimicrobial stewardship intervention combining telemedicine consultation, educational resources, and repeated point prevalence surveys (PPS).

Although PPS are well established as surveillance tools for monitoring antimicrobial prescribing in hospitals, little is known about whether repeated PPS themselves or followed educational feedback may influence prescribing behavior and contribute to sustained improvements in antibiotic stewardship [7,13–15].

Material and Methods

Study Population and Design

The TeleKasper intervention included a telemedical antimicrobial stewardship consultation service supported by a web- and smartphone-based application

(TeleKasper App) providing evidence-based infectious disease and antimicrobial treatment recommendations for physicians and pharmacists. This application worked as a textbook-style resource and additionally offered telemedical consultations and case conferences. Regular educational webinars on pediatric infectious diseases (PID) and antimicrobial stewardship (AMS) complemented the intervention. In brief, thirty-three non-university children's hospitals were organized into four regional networks guided by central reference hospitals with specialized PID expertise (Hubs). The non-university hospitals were randomized in clusters using a stepped-wedge design with a monthly run-in intervention phase for one to two hospitals. The study protocol has been published previously [16].

A standardized electronic case report form (CRF) was specifically developed for this study by PID specialists and clinical pharmacists to evaluate of ABT prescriptions concerning indication, 1st-line choice of ABT, and dosing [17]. The PPS CRF focused on non-intensive care wards and was pilot-tested over six months to ensure usability and data quality.

Between March 2022 and June 2024, ten PPS were conducted quarterly on non-intensive pediatric wards: one PPS (before run-in of the first hospital), eight during the step-wise implemented intervention phase, and one during the follow-up period. Due to the stepped-wedge design, the duration of intervention phase varied across hospitals, with a maximum of 23 months and a minimum of three months plus at least 3 months follow-up period [16]. Each hospital selected one survey day within a predefined four-week period. All patients receiving systemic antibiotic treatment at 8:00 a.m. on a pre-selected general pediatric wards were eligible after informed consent had been obtained. Following centralized quality and plausibility checks, patient identifiers were deleted by the participating hospitals. The PPS CRF and the checklist for plausibility check are provided in Supplements 10 and 11.

In each of the four hubs the CRF were reviewed by an expert panel of pediatricians and pharmacists with board qualification in infectious diseases. To ensure consistency across hubs, an initial review of 15 randomly selected and blinded cases from all hubs was conducted to test assessment comparability. Discrepancies were analyzed and discussed, leading to the development of standardized evaluation guidelines. The expert panel assessed treatment indication, antibiotic selection, combination therapy, route of administration, dosage, planned treatment duration, therapeutic drug monitoring, microbiological diagnostics, and therapy category (empirical, calculated, or targeted).

Assessments were based on national and international guidelines together with recommendations incorporated into the TeleKasper app. A dosing tolerance range of +/-20% (weight-based) was applied according to the app's recommendations. Missed microbiological diagnostics strongly recommended, such as drawing blood cultures in patients with sepsis or a urine culture in patients with pyelonephritis, led to the category “inappropriate diagnostics”. For the length of treatment, we evaluated the planned length of treatment (if documented by the prescriber) and the documented length of ABT up to the day of the PPS. The primary outcome ("*optimal care*") was defined as fulfillment of all three of the following criteria: indication (distinct clinical reason for ABT), recommended antibiotic, dosage according to the TeleKasper app.

Treatment duration was not included in the final analysis because therapy was often still ongoing in many patients at the time of PPS.

During the intervention phase, the expert panel of each Hub provided the participating hospitals with case-by-case feedback (educational feedback). Online conferences to discuss reported patients were also offered. In addition, physicians had access to online continuing education courses on key topics in PID during the intervention phase.

Thus, the TeleKasper intervention combined decision support, specialist consultation, educational activities, and structured audit-and-feedback.

For the data analysis, the hospitals were categorized according to size and urbanity. Pediatric departments were classified as small (up to 34 beds), medium (35 to 63 beds), and large (more than 63 beds). The definition of rural and urban region was based on the recommendation of the *German Federal Institute for Research on Building, Urban Affairs and Spatial Development* (Bundesinstitut für Bau-, Stadt- und Raumforschung, BBSR).

Following completion of the final PPS, participating hospitals were invited to complete a survey evaluating the acceptance of the intervention. The survey assessed respondents' satisfaction with the format of the expert feedback, whether the feedback was communicated to the treating physicians, and its perceived value for the management of subsequent patients (see Supplementary Table S8).

Statistical Analysis

Categorical variables are presented as frequencies and percentages and continuous variables as medians with interquartile ranges (IQR). The effect of the intervention on *optimal care* was analyzed using mixed-effects logistic regression models with hospital as a random effect. Three alternative models were compared: (i) an immediate change after the start of the intervention, (ii) an immediate change plus a continuous improvement with each PPS since the start of the intervention, and (iii) a continuous improvement with each PPS since the start of the intervention. Hospital size, calendar year and seasonality were included as fixed effects. Model fit was assessed using the Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC), and the model with the lowest BIC was selected for reporting (Supplementary Table S7). In addition, the association between the cumulative number of PPS conducted during the study period and *optimal care* assessed in PPS was evaluated in a separate mixed-

effects logistic regression model including hospital size and seasonality as fixed effects. Results are reported as odds ratios (OR) with 95% confidence intervals (CI). For descriptive purposes, prescribing quality during PPS 1–2 was compared with PPS 9–10. Statistical analyses were performed using R version 4.2 or later [18].

Ethical Approval

The study was approved by the Ethics Committee of the Ludwig Maximilians University Munich (project number 21-0500) and registered with the German Clinical Trials Register (DRKS00028534). Additionally, ethical approval was obtained from the local committees of the 3 participating universities (Hubs), as well as their respective German State Chambers of Physicians.

Results

Study population

Non-intensive care inpatient units of 33 pediatric hospitals participated in ten PPS rounds. Across the ten PPS, 5,241 children were hospitalized on participating non-intensive care wards, of whom 1,005 (19.2%) received antibiotic treatment. The median age was 3.67 years (IQR: 8.02 years).

Sufficient clinical information was available for 903 (89.9%) patients. After exclusion of patients receiving antimicrobial prophylaxis, 868 patients treated for active infection were included in the analysis. One patient received antibiotic treatment for both treatment and prophylaxis, resulting in a cohort of 868 patients treated for active infection (86.4% of all patients with antibiotic prescription). For further details of enrolled patient groups see Figure 1.

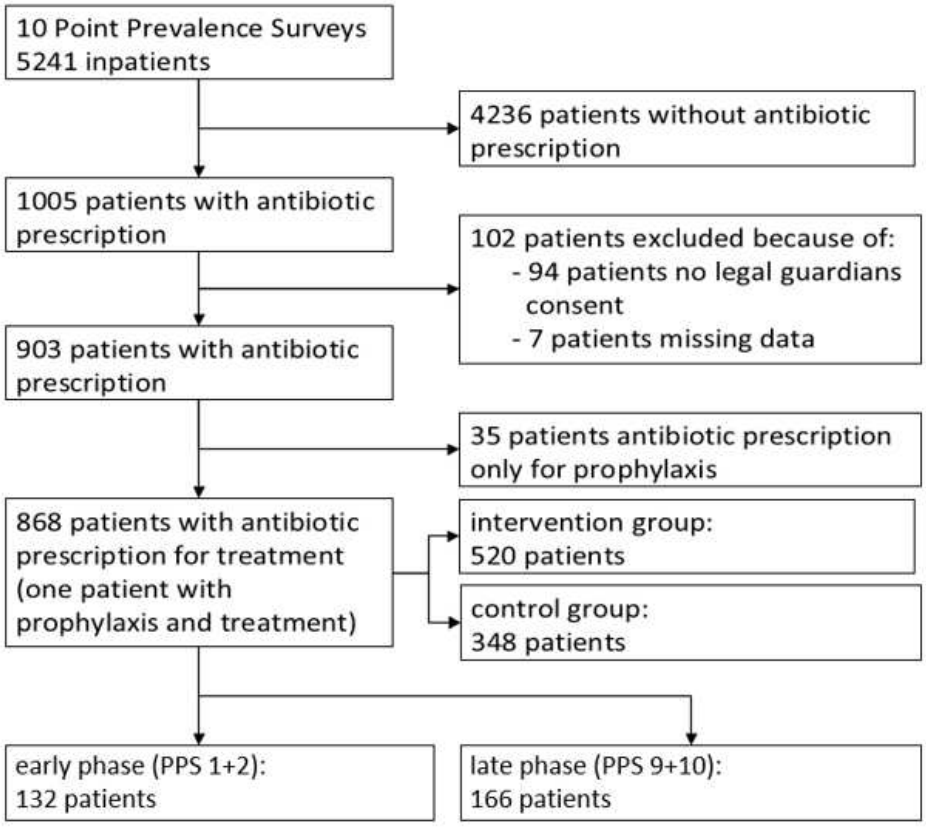


Figure 1. Participation Flowchart

Across ten point prevalence surveys (PPS), 5,241 hospitalized children were screened, of whom 1,005 (19.2%) received antibiotic treatment. After exclusion of 102 patients because of missing consent or incomplete data, and 35 because antibiotics were prescribed for prophylaxis. The final study population comprised 868 patients, including 520 (59.9%) in the intervention phase and 348 (40.1%) in the control phase. For the comparison of early versus late PPS, 132 patients from PPS 1-2 and 166 patients from PPS 9-10 were included.

The PPS data comprised 1,089 ABT prescriptions. Most patients (667; 76.8%) received monotherapy. Combination therapy consisted of two antibiotics in 182 patients (21.0%), three antibiotics in 18 (2.1%), and four antibiotics in one patient. In

906 cases (83.2%) ABT was administered intravenously. For Patient characteristics are summarized and recorded diagnoses (Supplementary Tables Tables S1 and S6).

Effects of TeleKasper intervention

Among the tested models, the model assuming a change at the start of the intervention provided the best fit according to the BIC criterion (see Supplementary Table S7). In this model, no effect of the start of the TeleKasper intervention on *optimal care* was observed (OR 0.74; 95% CI 0.47–1.17) (Table 1).

Table 1. Effects of introduction of TeleKasper intervention on *optimal care* measured in PPS (multivariable logistic regression additionally controlled for hospitals as random effect, OR>1 indicates improvement)

Variable	OR (95% CI)
Intervention	0.74 (0.47–1.17)
year 2023 vs. 2022	2.51 (1.57–4.00)
year 2024 vs. 2022	4.02 (2.20–7.36)
seasonality (May–September vs. October-April)	1.13 (0.84–1.54)
N of beds <35 vs. 35-63	1.17 (0.53–2.59)
N of beds >63 vs. 35-63	1.14 (0.53–2.45)

Results of a multivariable mixed-effects logistic regression model with hospital included as a random effect. Odds ratios >1 indicate higher odds of *optimal care*.

This conclusion also held for the alternative models (data not shown). Detailed quality parameters and antibiotic use comparing control and intervention are provided in Supplementary Tables S2 and S3.

At the same time, *optimal care* improved gradually over the course of the study, with comparable improvements observed during the control and intervention phase, on

average 14% per PPS (OR 1.14, 95% 1.07-1.20 per each PPS, see Table 2 and Figure 2, supplementary Table S9).

Table 2. Association of the cumulative number of conducted PPS with the optimal care measured in PPS (multivariable logistic regression, additionally controlled for hospitals as random effect, OR>1 indicates improvement

Variable	OR (95% CI)
PPS (per 1)	1.14 (1.07–1.20)
Seasonality (May–September vs. October-April)	1.00 (0.74–1.35)
N of beds <35 vs. 35-63	1.27 (0.58–2.77)
N of beds >63 vs. 35-63	1.19 (0.56–2.54)

Results of a multivariable mixed-effects logistic regression model with hospital included as a random effect. Odds ratios >1 indicate higher odds of *optimal care*.

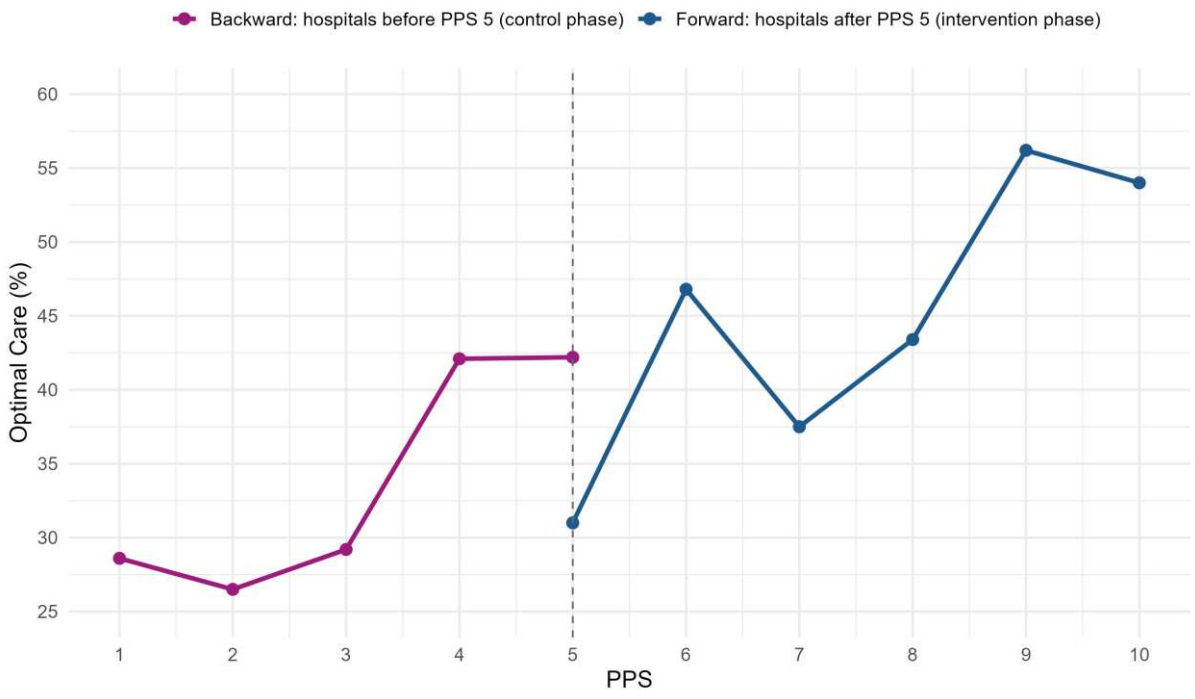


Figure 2. Association between repeated point prevalence surveys and prescribing quality

Optimal care was defined as the composite outcome of (i) an appropriate indication for antibiotic treatment, (ii) use of the recommended first-line antibiotic, and (iii) appropriate dosage according to the TeleKasper recommendations. The figure illustrates the proportion of patients receiving optimal care across ten consecutive PPS. Hospitals contributing observations before transition to the intervention are shown as "backward", whereas those contributing observations after transition are shown as "forward". Detailed data are provided in Supplementary Table S9.

The proportion of patients receiving *optimal care* increased from 25.8% in PPS 1–2 to 53.0% in PPS 9–10 (Table 3).

Table 3. Quality parameters summarized as *optimal care* in a comparison of early versus late PPS

Quality parameters		N (PPS 1+2)	% (95% CI, PPS 1+2)	N (PPS 9+10)	% (95% CI, PPS 9+10)
Treatment indicated	Yes	125	94.7 (90.9–98.5)	162	97.6 (95.3–99.9)
	No	7	5.3 (1.5–9.1)	4	2.4 (0.1–4.7)
Preferred antibiotic	Yes	85	64.4 (56.2–72.6)	130	78.3 (72.0–84.6)
	No	47	35.6 (27.4–43.8)	36	21.7 (15.4–28)
Recommended dosage	Yes	51	38.6 (30.3–46.9)	108	65.1 (57.8–72.3)
	No	81	61.4 (53.1–69.7)	58	34.9 (27.7–42.2)
Optimal care	Yes	34	25.8 (18.3–33.2)	88	53.0 (45.4–60.6)
	No	98	74.2 (66.8–81.7)	78	47.0 (39.4–54.6)

Comparison of early (first two PPS) and late (last two PPS) point prevalence surveys. For comparison of prescription quality, the three quality indicators were summarized as *optimal care.*

Effect on specific quality parameters

Compared with the first two PPS, last two PPS showed improvements in documentation of planned treatment duration (+9.5 percentage points [pp]), appropriate treatment duration (+16.4 pp), and microbiological diagnostics (+9.5 pp). The proportion of empirical, calculated, and targeted therapy remained unchanged, whereas cephalosporin use decreased by 14 pp (Supplementary Table S5). Sample sizes were insufficient for robust analyses of the remaining quality indicators (Supplementary Table S4).

Acceptance evaluation

Twenty-six (78.8%) of the 33 hospitals participated in the survey. Expert feedback was shared with treating physicians in 24 of 26 hospitals (92.3%). Twenty-five hospitals (96.2%) were satisfied with the format and scope of the educational feedback. Respondents from all participating hospitals agreed that repeated PPS together with expert feedback contributed to improving subsequent patient care. Further details are provided in Supplementary Table S8.

Discussion

Within this stepped-wedge trial with quarterly PPS assessments, we observed a progressive improvement in *optimal care* with each PPS. Improvements occurred both before and after initiation of the TeleKasper intervention in the participating hospitals. Overall, the proportion of patients classified in PPS as [receiving] *optimal care* did more

than double during the study period, corresponding to an absolute improvement of 27.3 pp. Although secular trends cannot be completely excluded, the magnitude and consistency of the observed improvement suggest that repeated PPS may have contributed to improved prescribing quality. These findings support the hypothesis that repeated PPS may themselves promote sustained improvements in prescribing behavior, an effect similar to the one intended and well established by clinical audits [19]. While the design did not allow to separate the potential impact of repeated PPS exposure in our study from the secular temporal trend, evidence from previous AMS studies indicates that audit- and feedback-based monitoring strategies can independently promote meaningful and sustained improvements in prescribing quality [20]. A recent Cochrane review of 140 trials across clinical areas found that such audit and feedback produces do have modest effect on improving patient care processes, with a median 4.3% absolute improvement in compliance with recommendation practice [21]. In our study, there was an improvement of 14% per one PPS (and cumulative improvement of 27.3% after 8-9 PPS). The unexpected observation was that the improvement was not restricted to the hospitals with already established intervention, but was very similar also in the control group (before the Telekasper project was started). This could be explained e.g. by the “Hawthorne effect”, whereby prescribing practices improve because participants become aware that their clinical practice is observed and evaluated [22, 23]. In addition, the structure of the PPS questionnaire itself may have influenced prescribing behavior by implicitly highlighting desirable AMS items (e.g. appropriate diagnostics, questions to dosing regimens etc.). Repeated participation may also have encouraged clinicians to reflect on previous prescribing decisions and apply this experience to subsequent patients. In contrast to earlier initiatives such as ARPEC (Antibiotic Resistance and Prescribing in European Children), where PPS assessments were typically performed as single surveys or at

longer intervals, repeated PPS performed at regular short intervals may lead to stronger learning and stewardship effects [19, 24].

All participating hospitals reported that expert feedback supported appropriate management of subsequent patients. This observation is consistent with previous antibiotic stewardship studies showing that audit-and-feedback approaches alone can positively improve future prescribing behavior and support sustained changes in clinical practice, albeit with a delay of several years in impact on the prescription quality [25, 26].

We did not observe an independent effect of structured PPS feedback, and the TeleKasper intervention itself. In our Study hospitals participated in the intervention phase for a mean duration of 15.7 months and educational interventions, e.g. PPS feedback, may require sustained implementation and stable clinical teams before measurable effects become apparent. Audit-and-feedback interventions are inherently delayed because recommendations can only influence subsequent prescribing decisions rather than those already assessed [17].

Several methodological limitations of our study should be acknowledged. Data collection relied exclusively on CRF-based documentation without access to individual patient records, which limited the ability to comprehensively assess therapeutic indications and treatment duration. The absence of additional clinical variables, such as disease severity, or laboratory findings, may have further reduced the precision of prescription quality assessments. Thus, assessment of treatment indication was often based solely on the recorded preliminary diagnosis. Further, appropriateness of treatment duration could not be finally evaluated in over 50% because treatment was still ongoing at the time of PPS. Future studies should therefore consider alternative methodological approaches, such as retrospective or prospective assessment of

completed events. Another important parameter that was not included in the assessment was the proportion of patients with infections who received supportive care alone or for whom ABT was intentionally withheld. Implementation in routine care will require streamlined workflows and sustainable technical infrastructure beyond the setting of a funded research project [27-29].

Despite these limitations, our study suggest that repeated PPS may serve not only as monitoring instruments but also as interventional tools capable of promoting behavioral change [30]. The combination of systematic assessment and educational feedback distinguishes the TeleKasper PPS approach from purely observational surveillance studies [31, 32]. The measurable improvements observed with respect to *optimal care* over time show the potential value of repeated, feedback-oriented surveillance strategies within pediatric ASP.

Nevertheless, considerable potential for further improvement remains, particularly regarding continuous educational feedback and the long-term integration of stewardship interventions into routine clinical practice [10]. The maximal achievable effect of this study design remains uncertain.

Whether these improvements are sustained after completion of the TeleKasper program remains unknown and should be evaluated in future follow-up studies.

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Data availability

The de-identified patient-level electronic health records and hospital-level antibiotic use density data used for this analysis was obtained from individual hospital organizations and cannot be shared publicly because permission for onward sharing was not granted by the participating hospitals. Access may be granted upon reasonable request, subject to approval by the participating hospitals. Requests should be directed to the corresponding author or by to Rafael Mikolajczyk (rafael.mikolajczyk@uk-halle.de).

Declarations

Conflict of interests

The study was funded by the German Federal Joint Committee (G-BA; grant number 01NVF19009). All authors declare no competing interests.

Ethics approval

The study was approved by the Ethics Committee of Ludwig Maximilian University Munich (reference no. 21-0500) and was registered in the German Clinical Trials Register (DRKS00028534). Additional ethical approval was obtained from the local ethics committees of all participating Hub institutions and the respective State Chambers of Physicians.

Consent to participate

Written informed consent was obtained from at least one legal guardian of each participating child before inclusion within a consultation in the study, in accordance with the requirements of the responsible ethics committees.

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Abbreviations

ABT, antibiotic treatment

AIC, Akaike Information Criterion

AMR, antimicrobial resistance

AMS, antimicrobial stewardship

ASP, antimicrobial stewardship program

BBSR, Federal Institute for Research on Building, Urban Affairs and Spatial Development

BIC, Bayesian Information Criterion

DRKS, German Clinical Trials Register

G-BA, Federal Joint Committee

IQR, interquartile range

LMU, Ludwig Maximilian University

LOT, length of treatment

OR, odds ratio

PID, pediatric infectious diseases

PPS, point prevalence survey

SD, standard deviation

TDM, therapeutic drug monitoring

References

1. GBD 2021 Antimicrobial Resistance Collaborators. Global burden of bacterial antimicrobial resistance 1990–2021: a systematic analysis with forecasts to 2050. Lancet. 2024;404(10459):1199–1226. https://doi.org/10.1016/S0140-6736(24)01867-1.
2. Duong QA, Pittet LF, Curtis N, Zimmermann P. Antibiotic exposure and adverse long-term health outcomes in children: a systematic review and meta-analysis. J Infect. 2022;85(3):213–300. https://doi.org/10.1016/j.jinf.2022.01.005.
3. Same RG, Amoah J, Hsu AJ, et al. Antibiotic-associated adverse events in hospitalized children. J Pediatric Infect Dis Soc. 2021;10(5):622–628. https://doi.org/10.1093/jpids/piaa173
4. Aversa Z, Atkinson EJ, Schafer MJ, et al. Association of infant antibiotic exposure with childhood health outcomes. Mayo Clin Proc. 2021;96(1):66–77. https://doi: 10.1016/j.mayocp.2020.07.019
5. Kolberg L, Khanijau A, et al. Raising AWaRe-ness of antimicrobial stewardship challenges in pediatric emergency care: results from the PERFORM study assessing consistency and appropriateness of antibiotic prescribing across Europe. Clin Infect Dis. 2024;78(3):526–534. https://doi.org/10.1093/cid/ciad6
6. Metsvaht T, Nellis G, Varendi H, et al. High variability in the dosing of commonly used antibiotics revealed by a Europe-wide point prevalence study: implications for research and dissemination. BMC Pediatr. 2015;15:41. https://doi.org/10.1186/s12887-015-0359-y
7. De Luca M, Donà D, Montagnani C, et al. Antibiotic prescriptions and prophylaxis in Italian children. Is it time to change? Data from the ARPEC

Project. PLoS One. 2016;11(5):e0154662. https://doi.org/10.1371/journal.pone.0154662

8. Versporten A, Bielicki J, Drapier N, et al. The antibiotic resistance and prescribing in European Children project: a neonatal and pediatric antimicrobial web-based point prevalence survey in 73 hospitals worldwide. Pediatr Infect Dis J. 2013;32(6):e242–e253. https://doi.org/10.1097/inf.0b013e318286c612
9. Probst V, Islamovic F, Mirza A. Antimicrobial stewardship program in pediatric medicine. Pediatr Investig. 2021;5(3):229–238. https://doi.org/10.1002/ped4.12292
10. Donà 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. https://doi.org/10.1186/s13756-019-0659-3
11. Grammatico-Guillon L, Abbis L, Thibault C, et al. Scope of antibiotic stewardship programs in pediatrics. Clin Pediatr (Phila). 2019;58(11–12):1291–1301. https://doi.org/10.1177/0009922819852985
12. Livorsi DJ, Ohl ME, Eells SJ, et al. An implementation roadmap for establishing remote infectious disease specialist support for consultation and antibiotic stewardship in resource-limited settings. Open Forum Infect Dis. 2022;9(12):ofac588. https://doi.org/10.1093/ofid/ofac588
13. Blinova E, Lau E, Bitnun A, et al. Point prevalence survey of antimicrobial utilization in the cardiac and pediatric critical care unit. Pediatr Crit Care Med. 2013;14(6):e280–e288. https://doi.org/10.1097/pcc.0b013e31828a846d
14. Papan C, Willrich N, Hufnagel M, et al. Antimicrobial use in pediatric oncology and hematology in Germany and Austria, 2020/2021: a cross-sectional, multicenter point-prevalence study with a multi-step qualitative adjudication

process. Lancet Reg Health Eur. 2023;28:100599. https://doi.org/10.1016/j.lanepe.2023.100599

15. Gharbi M, Doerholt K, Vergnano S, et al. Using a simple point-prevalence survey to define appropriate antibiotic prescribing in hospitalised children across the UK. BMJ Open. 2016;6(11):e012675. https://doi.org/10.1136/bmjopen-2016-012675
16. Diexer S, Mader S, Schlagenhauf A, et al. Telemedicine-based antibiotic stewardship program in pediatrics: study protocol of a stepped wedge cluster randomized trial—the TeleKasper study. Trials. 2024;25(1):678. https://doi.org/10.1186/s13063-024-08493-z
17. Spivak ES, Cosgrove SE, Srinivasan A. Measuring appropriate antimicrobial use: attempts at opening the black box. Clin Infect Dis. 2016;63(12):1639–1644. https://doi.org/10.1093/cid/ciw658
18. R Core Team. R: A language and environment for statistical computing. Vienna: R Foundation for Statistical Computing; 2024.
19. Pauwels I, Versporten A, Vermeulen H, Vlieghe E, Goossens H. Assessing the impact of the Global Point Prevalence Survey of Antimicrobial Consumption and Resistance (Global-PPS) on hospital antimicrobial stewardship programmes: results of a worldwide survey. Antimicrob Resist Infect Control. 2021;10(1):138. https://doi.org/10.1186/s13756-021-01010-w.
20. Sikkens JJ, van Agtmael MA, Peters EJG, et al. Behavioral approach to appropriate antimicrobial prescribing in hospitals: the Dutch Unique Method for Antimicrobial Stewardship (DUMAS) participatory intervention study. JAMA Intern Med. 2017;177(8):1130–1138. https://doi.org/10.1001/jamainternmed.2017.0946.

21. Pett RG, Silva F, D'Amico C. Audit and Feedback: A Quality Improvement Study to Improve Antimicrobial Stewardship. Fed Pract. 2021 Jun;38(6):276-281. doi: 10.12788/fp.0135. PMID: 34733075; PMCID: PMC8560048.
22. Chen LF, Vander Weg MW, Hofmann DA, et al. The Hawthorne effect in infection prevention and epidemiology. Infect Control Hosp Epidemiol. 2015;36(12):1444–1450. https://doi.org/10.1017/ice.2015.216
23. Mangione-Smith R, Elliott MN, McDonald L, et al. An observational study of antibiotic prescribing behavior and the Hawthorne effect. Health Serv Res. 2002;37(6):1603–1623. https://doi.org/10.1111/1475-6773.10482
24. Versporten A, Bielicki J, Drapier N, et al. The Worldwide Antibiotic Resistance and Prescribing in European Children (ARPEC) point prevalence survey: developing hospital-quality indicators of antibiotic prescribing for children. J Antimicrob Chemother. 2016;71(4):1106–1117. https://doi.org/10.1093/jac/dkv418
25. Chung GW, Wu JE, Yeo CL, Chan D, Hsu LY. Antimicrobial stewardship: a review of prospective audit and feedback systems and an objective evaluation of outcomes. Virulence. 2013;4(2):151–157. https://doi.org/10.4161/viru.21626.
26. Ray KN, Wittman SR, Kelly MK, et al. Primary care telemedicine vs in-person antibiotic prescribing for pediatric respiratory tract infections. JAMA Netw Open. 2026;9(5):e2610062. https://doi.org/10.1001/jamanetworkopen.2026.10062.
27. Young JD, Abdel-Massih R, Herchline T, et al. Infectious Diseases Society of America position statement on telehealth and telemedicine as applied to the practice of infectious diseases. Clin Infect Dis. 2019;68(9):1437–1443. https://doi.org/10.1093/cid/ciy907

28. Shively NR, Moffa MA, Paul KT, et al. Impact of a telehealth-based antimicrobial stewardship program in a community hospital health system. Clin Infect Dis. 2020;71(3):539–545. https://doi.org/10.1093/cid/ciz878
29. Dirjayanto VJ, Lazarus G, Geraldine P, et al. Efficacy of telemedicine-based antimicrobial stewardship program to combat antimicrobial resistance: a systematic review and meta-analysis. J Telemed Telecare. 2025;31(5):615–627. https://doi.org/10.1177/1357633X231204919
30. Meesters K, Chappell F, Demirjian A. Trends in antibiotic use in a large children's hospital in London (United Kingdom): 5 years of point prevalence surveys. Antibiotics (Basel). 2024;13(2):172. https://doi.org/10.3390/antibiotics13020172
31. Soltani J, Gharibi T, et al. Global-PPS targets for antimicrobial stewardship in paediatric patients at hospitals in Sanandaj, Western Iran, compared with Southeast Asian and European hospitals. J Glob Antimicrob Resist. 2024;36:473–481. https://doi.org/10.1016/j.jgar.2024.01.011
32. Akintan P, Adebisi YA, et al. Point prevalence surveys of antibiotic prescribing in children at a tertiary hospital in a resource-constrained, low-income sub-Saharan African country—the impact of an antimicrobial stewardship program. BMC Pediatr. 2024;24(1):383. https://doi.org/10.1186/s12887-024-04847-3

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