



OPEN Temporal trends in pediatric pharyngitis and antibiotic prescribing in Italian primary care from 2010 to 2024

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Pharyngitis is a major contributor to antibiotic overuse in paediatric primary care, thereby driving antimicrobial resistance. Distinguishing group A β -hemolytic streptococcus (GABHS) from non-specific pharyngitis is crucial, as it directly influences treatment decisions. Post-COVID-19 changes in infection patterns and prescribing behaviours have been observed. This study investigates the epidemiology, management, and outcomes of paediatric pharyngitis using data from the Pedianet network. Episodes of pharyngitis occurring between January 2010 and September 2024 among children aged 0–14 years were included and classified as GABHS, and in a heterogeneous category named non-specific pharyngitis. Antibiotic prescriptions within 14 days after the diagnosis were considered. Descriptive statistics, incidence rates, prescription rates, and logistic models were used to describe these patterns and evaluate the association between antibiotic use and access to Emergency Room (ER) or hospitalization for any cause within 15 days after the diagnosis. Results from logistic regression analyses were reported as odds ratios (ORs) and 95% confidence intervals (95% CIs). A total of 567,705 episodes of pharyngitis were included (18.8% GABHS and 81.2% non-specific pharyngitis). Pharyngitis mainly affected preschool and school-age children (43.5% and 25.9% in those aged 2–<6 and 6–<11 years, respectively), whereas non-specific pharyngitis also involved children younger than two years (27.5%). Overall incidence rates declined over time, except for GABHS pharyngitis in the post-COVID-19 period (7.22 events per 100 person-years). Almost all GABHS pharyngitis cases were treated, while a portion of non-specific pharyngitis cases remained untreated. Amoxicillin was the most prescribed antibiotic, but during and post-COVID-19 pandemic, broader-spectrum antibiotics were used more frequently than in the pre-pandemic period. Treatment in children diagnosed with non-specific pharyngitis was associated with a 49% (OR=1.49, 95%CI:1.33–1.66) significantly higher risk of access to ER or hospitalization for all cause, while no association was found in GABHS pharyngitis (OR=0.91, 95%CI:0.69–1.21). The post-COVID-19 incidence peak of pharyngitis may reflect an immunity gap among children. Guideline-based antibiotic use remains essential to prevent complications and antimicrobial resistance, thereby optimizing the management of pharyngitis.

Keywords Pharyngitis, Antibiotics, GABHS, Primary care, Children

Streptococcus pyogenes (group A β -hemolytic streptococcus, GABHS) is the leading cause of bacterial pharyngitis, accounting for approximately 15–30% of cases in children¹. Although school-aged children are most commonly affected, with incidence peaking around 7–8 years, infections may also occur in younger individuals.

International and national guidelines recommend the use of rapid antigen detection tests (RADTs) or throat culture for children presenting with clinical features consistent with GABHS pharyngitis and recommend antibiotic therapy only for microbiologically confirmed cases^{2,3}. Specifically, penicillin V and amoxicillin remain the recommended first-line treatments, as GABHS continues to exhibit universal susceptibility to penicillins

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in most settings⁴. Despite this recommendation, real-world antibiotic prescribing, especially in primary-care settings, for paediatric pharyngitis exceeds the prevalence of GABHS infections, leading to a persistent inappropriate misuse of broad-spectrum antibiotics⁵. Unnecessary antibiotic use in non-bacterial pharyngitis is associated with increased adverse events and higher healthcare costs, contributing to the development of antimicrobial resistance⁶.

During the COVID-19 pandemic, antibiotic prescriptions declined by nearly 80% for respiratory infections, largely due to containment measures such as school closures, reduced social contact, and widespread mask use, which drastically lowered the circulation of common respiratory pathogens⁷. Despite a marked reduction in prescribing volume, antibiotic appropriateness did not substantially improve, with continued use of broad-spectrum agents, likely reflecting diagnostic uncertainty, particularly during remote consultations⁸.

Moreover, in the post-pandemic years, efforts to improve prescribing appropriateness have been further challenged by recurrent shortages of first-line antibiotics. These shortages, partly stemming from COVID-19-related disruptions to global supply chains, together with manufacturing delays and regulatory constraints, have affected the availability of essential agents such as amoxicillin⁹. The European Medicines Agency (EMA) has also reported widespread shortages of antibiotics commonly used to treat respiratory infections¹⁰. As a result, physicians have often been forced to prescribe alternative broader-spectrum agents.

This study aimed to investigate temporal trends in GABHS and non-specific pharyngitis, antibiotic prescribing patterns, and the association between antibiotic prescribing and emergency department admissions and hospitalizations among Italian children from 2010 to 2024.

Materials and methods

Data source

Children were enrolled from the primary care Pédianet database (<http://www.pedianet.it>), an independent network of more than 250 family paediatricians (FPs) using the Junior Bit® software in their clinical practice. The database collects demographic, clinical, and prescription data from children whose parents or legal guardians have provided informed consent and are under the care of participating FPs. Data generated during routine clinical practice are validated and stored anonymously in compliance with Italian regulations at a secure data repository in Padova (Veneto region). Pédianet represents approximately 4% of the annual national paediatric population, as previously described¹¹.

Study design and study population

This retrospective population-based cohort study included episodes of pharyngitis occurring among children aged 0–14 years between January 2010 and September 2024 who were followed by one of the FPs belonging to the Pédianet network. Children were included only if they adhered to the well-child visits schedule recommended by the national healthcare system, to minimize person-time, exposure, and outcome misclassification¹². Children entered the follow-up on January 1, 2010, the date of starting care with a Pédianet FP or birth, whichever occurred last, and ended the follow-up on September 22, 2024, the date of leaving assistance or reaching 15 years of age, whichever occurred first.

Pharyngitis cases were identified using the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) or, if reported as free-text in the medical charts, using a research string under the supervision of a clinical data manager to maximize accuracy and reduce misclassification (Table S1).

To avoid counting follow-up visits as new infectious episodes, we applied a time-based visit-cleaning algorithm previously described in earlier Pédianet research⁷. Specifically, the first visit with a pharyngitis diagnosis was considered the index (incident) episode, whereas all visits occurring within the subsequent 15 days were classified as follow-up visits and removed from the analysis. This approach ensures that only distinct infectious events were included and it reduced bias due to repeated consultations for the same illness episode.

Pharyngitis diagnoses were classified as (i) GABHS pharyngitis if specifically reported in the diagnosis fields or if a positive RADT was recorded within ± 2 days of the diagnosis; and (ii) non-specific pharyngitis in all other cases, including non-GABHS, non-specified and rhinopharyngitis. This latter category does not necessarily represent confirmed viral infection or inappropriate antibiotic indication, as it may also include untested, miscoded, or clinically uncertain cases.

Exposure definition

All prescriptions referring to the Anatomical Therapeutic Chemical (ATC) code J01* within 14 days after the infection were collected. Prescriptions were deduplicated by ATC and date. Antibiotics were classified according to the 2023 World Health Organization (WHO) Access, Watch, and Reserve (AWaRe) classification¹³ (Table S2).

Outcome definition

The outcome of interest was any all-cause emergency department visit or hospitalization occurring within 15 days after the diagnosis. Outcome data were obtained from hospital discharge letters (available from 2017 onward in the Veneto Region), which, for children whose parents provided informed consent, are automatically integrated into the electronic medical records of Pédianet FPs. To ensure complete and accurate outcome assessment, this analysis was restricted to pharyngitis cases recorded from 2017 forward among children residing in the Veneto region with documented informed consent.

Statistical methods

Sociodemographic characteristics of children with GABHS and non-specific pharyngitis (i.e., sex, age at diagnosis, and Area Deprivation Index [ADI] as a proxy for the socioeconomic status¹⁴) and clinical characteristics of cases were summarized using frequencies and percentages and medians and interquartile ranges, for categorical

and continuous variables, respectively. The chi-square test and Wilcoxon rank-sum test were used to assess differences among types of pharyngitis. Diagnoses were described using annual incidence rates (IRs) per 100 person-years, with corresponding 95% confidence intervals (CIs), overall and stratified by age at diagnosis. Antibiotic prescriptions were described through annual prescription rates (PRs) (i.e., the number of pharyngitis episodes treated with at least one antibiotic divided by the total number of pharyngitis episodes) with 95% CIs, overall and by AWaRe classification. In addition, for confirmed GABHS pharyngitis, prescription rates of amoxicillin and amoxicillin-clavulanate were calculated for the first episode. Logistic regression models were adjusted for sex, age at diagnosis, Area Deprivation Index (ADI), number of outpatient visits in the previous year, and number of antibiotic prescriptions in the previous year, used as proxies of baseline healthcare utilization patterns (i.e. only pharyngitis with at least one year of retrospective follow-up were included in the analysis), and accounted for within-subject correlation. We followed the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) guidelines. The significance level was set at 0.05 and all statistical analyses were performed using SAS software, version 9.4 (SAS Institute, 17 Inc., Cary, NC, USA) and R version 4.4.2 (2024-10-31 ucrt).

This study was conducted in accordance with the tenets of the Declaration of Helsinki and was compliant with the European Network of Centres for Pharmacoepidemiology and Pharmacovigilance's Guide on Methodological Standards in Pharmacoepidemiology. The Internal Scientific Committee of Società Servizi Telematici Srl, the legal owner of Pedianet, approved the study and access to the database. According to Italian law, observational, retrospective, non-interventional studies do not require the approval by an ethics committee in Italy.

Results

A total of 567,705 pharyngitis episodes were included, of which 18.8% were classified as GABHS pharyngitis and 81.2% as non-specific pharyngitis. Pharyngitis predominantly affected preschool and school-aged children, with 43.5% of cases occurring among those aged 2 to <6 years and 25.9% among those aged 6 to <11 years. Cases were relatively evenly distributed across ADI categories, although a slightly higher proportion was observed in the intermediate group (19.2%). Non-specific pharyngitis was also frequent among children younger than 2 years (27.5%). The proportion of episodes treated with antibiotics was substantially higher for GABHS than for non-specific pharyngitis (91.7% vs 44.4%). No significant difference by sex was observed between groups (Table 1).

The incidence of pharyngitis declined over time, with a marked drop during the COVID-19 period (from 5.71 to 0.99 and from 23.30 to 7.98 per 100 person-years for GABHS and non-specific pharyngitis, respectively). However, GABHS pharyngitis rebounded after the COVID-19 pandemic, reaching 7.22 cases per 100 person-years in 2023, exceeding rates observed before the COVID-19 pandemic (Fig. 1). Similar age-related trends were observed, with GABHS rates highest among children aged 2–<6 years, followed by those aged 6–<11 years, whereas non-specific rates peaked among those <2 years (Figure S1–Panel A, Figure S1–Panel B).

	Overall pharyngitis	GABHS ^a pharyngitis	Non-specific pharyngitis	P-value
	N = 567,705	N = 106,601	N = 461,104	
Sex				
Male	296,975 (52.3)	55,832 (52.4)	241,143 (52.3)	0.6464
Female	270,730 (47.7)	50,769 (47.6)	219,961 (47.7)	
Age, median (IQR ^b)	4.3 (2.2 - 7.3)	6 (4.2 - 8.5)	3.8 (1.8 - 6.8)	<.0001
0-<2 years	130,841 (23)	3,812 (3.6)	127,029 (27.5)	<.0001
2-<6 years	246,894 (43.5)	49,850 (46.8)	197,044 (42.7)	
6-<11 years	147,053 (25.9)	43,640 (40.9)	103,413 (22.4)	
11-<15 years	42,917 (7.6)	9,299 (8.7)	33,618 (7.3)	
Area Deprivation Index				
Least deprived - 1	82,378 (14.5)	18,880 (17.7)	63,498 (13.8)	<.0001
2	92,904 (16.4)	20,077 (18.8)	72,827 (15.8)	
3	108,775 (19.2)	20,046 (18.8)	88,729 (19.2)	
4	101,048 (17.8)	18,911 (17.7)	82,137 (17.8)	
Most deprived - 5	94,182 (16.6)	15,879 (14.9)	78,303 (17)	
Missing ^c	88,418 (15.6)	12,808 (12)	75,610 (16.4)	
At least an antibiotic prescription	302,309 (53.3)	97,743 (91.7)	204,566 (44.4)	<.0001
At least an Access prescription*	205,249 (67.9)	76,765 (78.5)	128,484 (62.8)	<.0001
At least a Watch prescription*	106,596 (35.3)	23,705 (24.3)	82,891 (40.5)	<.0001
At least a Reserve prescription*	1 (0.0)	0 (0.0)	1 (0.00)	1.0000

Table 1. Sociodemographic and clinic characteristics overall and by type of pharyngitis. ^a Group A β -hemolytic streptococcal. ^b Interquartile range. ^c Missing values are considered itself as a level because it includes both newborns without a defined area deprivation index, or children with a mistaken/missing address. *Calculated by considering as denominator the number of episodes with at least an antibiotic prescription.

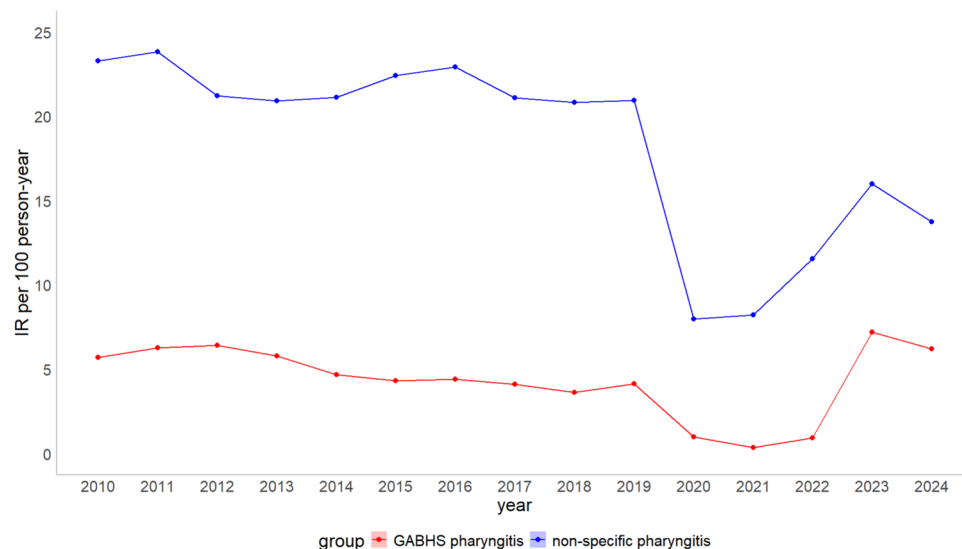


Fig. 1. Annual Incidence Rates (IRs) and 95% Confidence Intervals (95% CIs) of pharyngitis expressed in 100 person-year, stratified by type of pharyngitis.

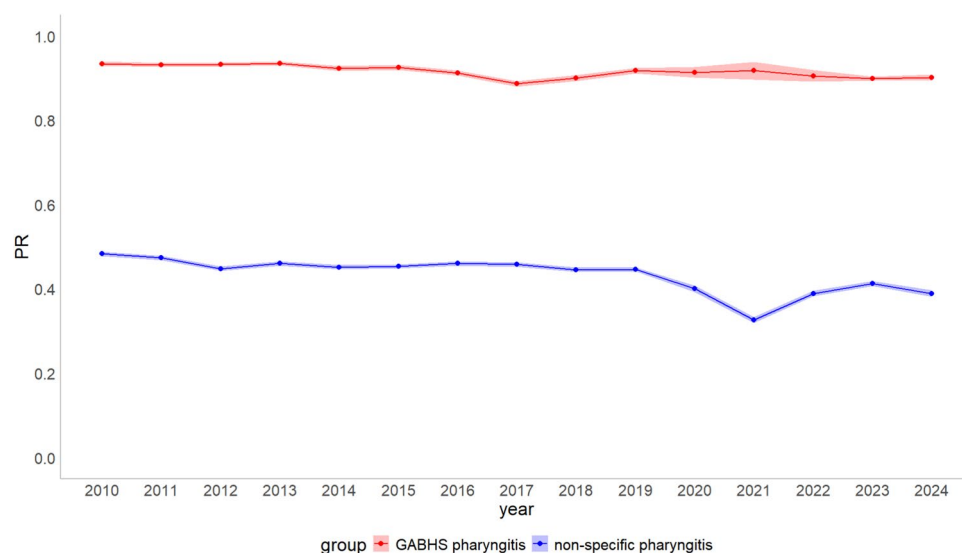


Fig. 2. Annual antibiotic Prescription Rates (PRs) and 95% Confidence Intervals (95% CIs), stratified by type of pharyngitis.

The PRs for GABHS pharyngitis remained close to one throughout the study period, indicating that nearly all cases were treated with at least one antibiotic (median PR=0.92). In contrast, a portion of non-specific pharyngitis remained untreated, with the lowest PR observed in 2021 (PR=0.33). Overall, the PR for non-specific cases slightly decreased over time, from 0.48 to 0.39 (Fig. 2).

Before the COVID-19 pandemic, among GABHS pharyngitis episodes, the use of Access antibiotics showed a slight increase (PR from 0.67 to 0.75), while the use of Watch antibiotics slightly decreased (PR from 0.28 to 0.19); however, this pattern reversed during 2020–2021 (Access PR=0.64 and Watch PR=0.30 in 2021), corresponding to the COVID-19 period (Figure S1–Panel C). Conversely, among non-specific pharyngitis, the use of Access antibiotics decreased from 2017 onward, whereas the use of Watch antibiotics declined across the entire study period; both Access and Watch antibiotic prescriptions reached notable lows in 2021 (Figure S1–Panel D). Focusing on amoxicillin versus amoxicillin–clavulanate for the first confirmed GABHS episode, amoxicillin was consistently the most prescribed antibiotic (median PR = 0.49), whereas amoxicillin–clavulanate remained consistently low throughout the study period (median PR = 0.26) (Figure S2).

When evaluating the impact on all-cause ER admission and hospitalization, 77,325 episodes recorded in the Veneto region were included, of which 23,685 (30.6%) were due to GABHS. No statistically significant association was observed between antibiotic treatment and the risk of all-cause ER admission or hospitalization among

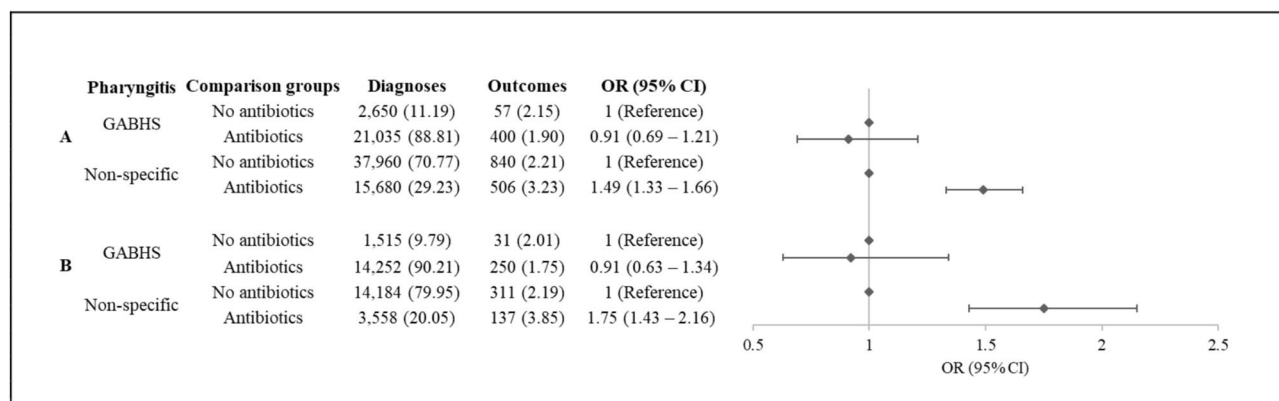


Fig. 3. Odds Ratios (ORs) and 95% Confidence Intervals (CIs) for the association between antibiotic treatment and access to emergency room or hospitalization within 15 days after the diagnosis, stratified by type of pharyngitis. Panel A shows results of the main analysis and Panel B shows results of the sensitivity analysis (i.e., restricting to RADT-confirmed GABHS pharyngitis). Models have been adjusted for sex, age at diagnosis and area deprivation index. Veneto cohort.

children with GABHS pharyngitis (OR=0.91, 95%CI: 0.69–1.21). Although treated children had an estimated 9% lower risk of the outcome, the confidence interval was compatible with both a potential protective association and no meaningful association. In contrast, among non-specific pharyngitis, antibiotic use was associated with a 49% higher risk of the outcome (OR=1.49, 95%CI: 1.33–1.66) (Fig. 3–Panel A). Furthermore, older age was associated with a lower risk of the outcome in both GABHS and non-specific pharyngitis compared with children aged 0–<2 years. Greater area-level deprivation was associated with a higher risk of the outcome, with a statistically significant association observed for GABHS pharyngitis (OR=1.26, 95% CI: 1.04–1.54) (Table S3). These findings were consistent in the sensitivity analysis restricted to RADT-confirmed GABHS pharyngitis, where GABHS-treated cases had a 9% lower risk (OR=0.91, 95%CI: 0.63–1.34) and non-specific treated cases had a 75% higher risk (OR=1.75, 95%CI: 1.43–2.16) of the outcome (Fig. 3–Panel B).

Discussion

In this primary care paediatric cohort, more than half a million pharyngitis cases were recorded in Italy between 2010 and 2024. Approximately one in five episodes was identified as GABHS, whereas the majority were non-specific. Despite this distribution, antibiotic prescribing remained high, with roughly half of non-specific pharyngitis cases being treated with an antibiotic. During the COVID-19 pandemic, pharyngitis incidence declined, followed by a GABHS rebound that exceeded pre-pandemic levels. Inappropriate prescribing practices persisted throughout the study period, with Watch antibiotics prescribed for almost 19% of episodes. Notably, antibiotic treatment in non-specific cases was associated with a higher risk of all-cause ER admission and hospitalization, whereas in GABHS pharyngitis, the association did not reach statistical significance, despite a protective role.

Our results aligned with the previously published literature. We found that 18.8% of pharyngitis cases were classified as GABHS cases, as reported in an Italian intersociety consensus published in November 2024, which estimated that GABHS accounts for approximately 10–20% of acute pharyngitis cases¹⁵. Furthermore, the observed decline during the COVID-19 period reflects trends reported in Italian, European, and North American studies, driven by lockdowns, social distancing, and the use of personal protective equipment, which substantially reduced the circulation of common respiratory pathogens^{16–19}. Similarly, the observed rebound in 2023 and 2024 aligned with an epidemiological alert from the European Centre for Disease Prevention and Control (ECDC), which reported an unexpected increase in GABHS infections after the lifting of pandemic restrictions²⁰.

Despite international guidelines recommending antibiotics only for confirmed cases of GABHS pharyngitis^{3,21}, our results showed that a higher proportion of non-specific cases continued to receive antibiotics. Similar prescribing patterns have also been reported in other countries, including the United States, where the number of antibiotic prescriptions for pharyngitis exceeds the expected prevalence of bacterial infections²². Several factors may contribute to the misuse of antibiotics in this context: diagnostic uncertainty due to limited use of RADTs as a standard of care, and parental pressure from a culture in which antibiotics are needed for any cause^{23,24}.

According to our results, considering the AWaRe classification, the widespread use of Watch antibiotics underscores the need for targeted stewardship programs. Although Access was the most prescribed, approximately one-third of cases also received a Watch antibiotic, consistent with previous studies indicating the use of macrolides and broad-spectrum antibiotics even when narrower ones are preferable^{15,25}. The narrowing gap observed during the COVID-19 years between Access and Watch may be attributed to changing care pathways and an amoxicillin shortage^{26,27}. Our analysis focusing on first episodes of confirmed GABHS pharyngitis showed that prescription rates of amoxicillin–clavulanate remained relatively lower but stable and relevant over time, despite guidelines recommending amoxicillin as the first-line therapy.

Our findings on all-cause emergency department attendance or hospitalization according to antibiotic use, stratified by GABHS and non-specific pharyngitis, showed that, although no significant association was observed in GABHS, a positive association was found in the non-specific pharyngitis group. Confounding by severity may explain this association, as children presenting with a worse clinical profile or without a clearly defined etiology may be more likely to receive antibiotics, some of which may not be indicated per guideline recommendations, and to be referred to higher levels of care. Given the observational design, the potential for confounding by indication and severity, and the all-cause nature of the outcome, this association should be interpreted as hypothesis-generating rather than evidence of a causal effect of antibiotic treatment on ED attendance or hospitalization. These findings suggest that, in the outpatient setting, antibiotics are often unnecessary for non-specific pharyngitis and may expose children, particularly younger ones, to avoidable adverse events and disruption of the microbiome²². Moreover, older age was associated with a lower risk of the outcome, consistent with known age-related differences in immune response and health susceptibility²⁸.

This study strongly supports the need to promote the rational use of antibiotics, especially in paediatric primary care settings. Introducing RADT as a standard of care could improve diagnostic accuracy and reduce inappropriate prescribing^{29,30}. Interventions targeting both FPs and parents, alongside stewardship programs may help align guideline recommendations with real-world needs.

This study has several strengths. It used data from FPs' primary care ambulatory settings, ensuring representativeness of the paediatric population and achieving a notable sample size. The 14-year time span allowed us to capture the variations attributable to new guidelines, health policies, antibiotic shortages, and the impact of the COVID-19 pandemic. The direct provision of ER and hospitalization data, through discharge letters automatically incorporated into the Pédianet electronic medical records, provided a comprehensive view of the burden of pharyngitis and its implications for antibiotic prescribing appropriateness. However, several limitations should be acknowledged. First, the classification of GABHS pharyngitis based solely on diagnostic labels may not capture the true etiology of the infection in the absence of microbiological confirmation. Nevertheless, sensitivity analyses restricted to RADT-confirmed cases yielded estimates consistent with the main findings, supporting the robustness of our results. Second, we were unable to account for heterogeneity in prescribing behaviour across family paediatricians, as the model could not incorporate a random intercept to adjust for clustering at the provider level. Third, outcome assessment, available only for a subset of children, may have introduced selection bias. Moreover, the outcome was defined as any emergency department visit or hospitalization within 15 days, regardless of cause; therefore, it does not allow us to isolate events directly attributable to pharyngitis. However, the observed outcome patterns align with evidence from previous Pédianet-based research and with findings reported in other settings, reinforcing confidence in the validity of the data. Finally, residual confounding may still affect our estimates. Although we adjusted the models for proxies of baseline clinical severity and healthcare utilization (including outpatient visits and antibiotic prescriptions in the previous year), children with a more severe clinical presentation may still have been more likely both to receive antibiotics and to access higher levels of care. As with all observational studies, residual confounding from unmeasured factors cannot be entirely ruled out.

Conclusion

This large primary-care cohort provides real-world evidence of changing paediatric pharyngitis epidemiology and persistent antibiotic overuse in Italy, particularly for non-specific pharyngitis. The post-pandemic rebound in GABHS diagnoses and the continued use of Watch antibiotics highlight the need for strengthened diagnostic stewardship, broader implementation of RADT-based pathways, and targeted antimicrobial stewardship in paediatric primary care.

Author' contributions

Guarantors, RB, AC accepts full responsibility for the finished work and/or the conduct of the study, had access to the data, and controlled the decision to publish; Conceptualization, RB, AC; Data Curation and Formal Analysis, RB, VR, FL; Writing – original draft preparation, RB, VR, AC; Writing – review and editing, GB, DD, CG.

Data availability

The data supporting this study's findings are available on request from the corresponding author (RB). The data are not publicly available due to restrictions (containing information that could compromise the privacy of research participants).

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Author contributions

Guarantors, RB, AC accepts full responsibility for the finished work and/or the conduct of the study, had access to the data, and controlled the decision to publish ;Conceptualization, RB, AC;Data Curation and Formal Analysis, RB, VR, FL;Writing – original draft preparation, RB, VR, AC;Writing – review and editing, GB, DD, CG.

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Declarations

Competing interests

The authors declare that the research was conducted without commercial or financial relationships that could be construed as potential conflicts of interest. The authors have no conflict of interest to declare. We affirm that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained. The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of any organization or company.

Ethics

This is an observational, retrospective, non-interventional study. According to a bylaw on the classification and implementation of observational drug-related research, as issued by the Italian National Drug Agency (an entity belonging to the Italian Ministry of Health), this study does not require approval by

an ethics committee in Italy (Italian Drug Agency note on August 3, 2007). This study was conducted in accordance with the tenets of the Declaration of Helsinki and was compliant with the European Network of Centres for Pharmacoepidemiology and Pharmacovigilance's Guide on Methodological Standards in Pharmacoepidemiology. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

Consent for publication

The study and access to the database was approved by the Internal Scientific Committee of So.Se.Te. Srl, the legal owner of Pedianet. The corresponding author confirm that he had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Additional information

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