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RSV Detection and Antibiotic Prescribing Decisions for Pediatric Respiratory Tract Infections

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Abstract

IMPORTANCE Respiratory syncytial virus (RSV) is a leading cause of pediatric viral lower respiratory tract infections (VLRTIs), often leading to inappropriate antibiotic use. Although rapid antigen diagnostic tests (Ag-RDTs) support clinical diagnosis, their effect on antibiotic prescribing in community settings remains uncertain.

OBJECTIVE To evaluate the association of RSV Ag-RDT implementation with antibiotic prescribing practices for infants and children assessed for LRTIs.

DESIGN, SETTING, AND PARTICIPANTS This retrospective cohort study used data from a community-based primary care setting involving family pediatricians in Italy participating in the Pedianet network. Data were collected between December 2023 and May 2024 from children aged 9 to 36 months with symptoms of VLRTI who underwent RSV Ag-RDT during the 2023-2024 respiratory epidemiologic season and historical matched cohorts.

EXPOSURE Children with RSV-positive and RSV-negative Ag-RDT results were compared with each other and with matched historical (2022-2023) and contemporaneous (2023-2024) cohorts of children with clinically diagnosed VLRTIs or bronchiolitis who did not undergo laboratory testing.

MAIN OUTCOMES AND MEASURES The primary outcome was antibiotic prescribing within 14 days of diagnosis. Prescriptions associated with suspected or confirmed bacterial infections (such as elevated C-reactive protein levels or documented coinfections) were excluded. Relative risks (RRs) and 95% CIs were estimated using log-binomial regression models.

RESULTS Among 256 cases (median age, 15.06 [IQR, 11.61-22.72] months; 133 males [51.95%]), 79 (30.86%) were RSV positive and 177 (69.14%) were RSV negative. These 2 groups were comparable in age, with RSV-negative children slightly younger (median age, 14.95 [IQR, 11.66-22.67] vs 15.34 [IQR, 11.40-23.10] months), and in sex distribution, with a higher proportion of females among RSV-positive cases (41 [51.90%] vs 82 [46.33%]). Antibiotic prescribing was lower in RSV-positive than RSV-negative children (0.18 [95% CI, 0.10-0.25] vs 0.29 [95% CI, 0.22-0.35] prescriptions per 10 person-days) and was associated with a reduction in risk of receiving an antibiotic prescription (RR, 0.52; 95% CI, 0.33-0.83). Implementation of RSV Ag-RDT was associated with lower antibiotic use for VLRTIs compared with a matched untested cohort (RR, 0.54 [95% CI, 0.44-0.66] in 2022-2023 and 0.61 [95% CI, 0.50-0.75] in 2023-2024) and for bronchiolitis in 2022-2023 (RR, 0.56 [95% CI, 0.33-0.95]) but not in 2023-2024 (RR, 0.75 [95% CI, 0.42-1.33]). Reductions were greater among RSV-positive cases: for VLRTIs, the RR was 0.33 (95% CI, 0.20-0.52) in 2022-2023 and 0.41 (95%

(continued)

Key Points

Question Are respiratory syncytial virus (RSV) antigen rapid diagnostic tests (Ag-RDTs) in primary care associated with reduced inappropriate antibiotic prescribing in children with suspected viral lower respiratory tract infections (VLRTIs), including bronchiolitis?

Findings In this cohort study of 256 children aged 9 to 36 months in Italy, implementing RSV Ag-RDTs in clinical practice was associated with a reduction in unnecessary antibiotic use. Overall, RSV Ag-RDTs were associated with a mean reduction in antibiotic prescribing for VLRTIs and bronchiolitis compared with clinically diagnosed cohorts.

Meaning The findings suggest incorporating RSV Ag-RDTs into pediatric care may support more appropriate antibiotic prescribing and could help reduce antibiotic overuse.

+ Invited Commentary

+ Supplemental content

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Abstract (continued)

CI, 0.25-0.67) in 2023-2024; for bronchiolitis, the RR was 0.33 (95% CI, 0.15-0.76) in 2022-2023, but the reduction was not significant in 2023-2024 (RR, 0.43 [95% CI, 0.18-1.00]).

CONCLUSIONS AND RELEVANCE In this cohort of 256 VLRTI cases, the findings suggest that RSV contributed to a broad range of VLRTIs across ages and that RSV Ag-RDT was a useful outpatient antimicrobial stewardship tool, particularly in bronchiolitis. Combined with universal immunoprophylaxis, widespread Ag-RDT use may improve diagnostic accuracy, resource allocation, and clinical outcomes.

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Introduction

Respiratory syncytial virus (RSV) is one of the leading causes of viral lower respiratory tract infections (VLRTIs), particularly bronchiolitis in infants and pneumonia in older children. Worldwide, RSV is estimated to cause approximately 33 million episodes of VLRTIs annually.[1,2] It is detected in 50% to 80% of children aged 0 to 5 years hospitalized with bronchiolitis, with the highest detection rates (up to 80%) observed in infants aged up to 12 months.[3] Additionally, RSV is identified in approximately 40% of children older than 12 months hospitalized with pneumonia.[4] The burden of RSV-related illness is particularly evident in community settings, where most infections occur and often remain undetected due to limited testing availability and the predominance of milder symptoms that do not require hospitalization.[1] Although factors such as prematurity, chronic lung disease, and congenital heart defects are known to be associated with increased risk of severe RSV infection, the absence of specific determinants to reliably predict which children will develop severe complications remains a major public health challenge.[5]

Despite established guidelines and ongoing antimicrobial stewardship efforts, antibiotics remain frequently prescribed for VLRTIs such as bronchiolitis and interstitial pneumonia.[6] In many cases, the overuse of antibiotics is influenced by symptom severity and physician perception, particularly in younger children. Focusing specifically on RSV bronchiolitis, a study from Israel reported that 33% (95% CI, 30.5%-36.4%) of hospitalized children with RSV bronchiolitis, without evidence of bacterial coinfections, were treated with antibiotics between 2008 and 2018.[7] A study published in 2020, based on a nationally representative US database spanning 2006 to 2015, found that antibiotics were prescribed in almost 60% of outpatient encounters for bronchiolitis and bronchitis. Prescription rates were notably higher in primary care settings (60.9%) compared with pediatric emergency departments (40.3%).[8] In another study conducted in Finland by Thomas et al,[9] 70.9% of infants with RSV infection treated in outpatient settings received an antibiotic prescription, underscoring the extent of inappropriate antibiotic use. This issue is particularly pronounced in community settings, where overlapping signs and symptoms of viral and bacterial infections, combined with limited access to diagnostic testing, often lead to diagnostic uncertainty.[7]

In recent years, the widespread use of rapid antigen diagnostic tests (Ag-RDTs) during the COVID-19 pandemic drove the advancement and adoption of rapid diagnostic tools for RSV, featuring improved performance characteristics.[10] These tools aim to improve diagnostic accuracy and potentially reduce unnecessary antibiotic use.[11] Although rapid tests are increasingly adopted in pediatric settings, evidence of their association with antibiotic prescribing for children in community settings remains scarce in the current literature. This study aimed to evaluate the association of RSV Ag-RDT implementation with antibiotic prescribing practices in pediatric primary care in Italy, specifically assessing whether its use was associated with reduced antibiotic prescriptions among both tested and clinically diagnosed VLRTI cases.

Methods

Data Source

This cohort study used data from Pedianet,[12] an independent network of over 200 Italian family pediatricians (FPs) who use the Junior Bit software[13] in their clinical practice, creating a pediatric primary care database. Covering around 4% of the yearly Italian pediatric population, the network collects data on demographics, health status, symptoms, prescriptions, and outpatient diagnoses. Written informed consent was provided, and all data were anonymized according to Italian regulations and stored securely in a protected cloud environment, identified only by unique numerical codes.[14] The Pedianet Internal Scientific Committee and the institutional review board of Società Servizi Pediatrici in Padova, Italy, approved this study. We followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline.

Cohort Selection

The data for this analysis were obtained from the Evolute study (conducted within the Pedianet network and described in detail in the eAppendix in Supplement 1) and the broader Pedianet database. In brief, the Evolute study was a prospective observational study in Veneto, Italy, assessing Ag-RDTs for RSV, influenza, and COVID-19 in children aged 9 to 36 months with LRTIs between December 2023 and May 2024 (the Evolute cohort). It involved 26 pediatricians and collected data on epidemiology, clinical management, costs, and quality of life for patients and caregivers.

Main Cohort

The main cohort of the current study consisted of cases (ie, statistical units) of children enrolled in the Evolute cohort who had negative test results for all 3 viruses and those who had a positive test result for RSV alone. Cases with indeterminate results or positive results for influenza A or B and/or SARS-CoV-2 infection were excluded.

Comparison Cohorts

The comparison cohorts included cases of children aged 9 to 36 months who were residents in northern and central Italy (excluding southern Italy due to differing viral circulation patterns) with clinical diagnoses based on signs and symptoms of bronchiolitis (bronchiolitis cohort) or VLRTI (VLRTI cohort). These cases were collected during the epidemiologic seasons from November 2022 to April 2023 and November 2023 to April 2024. All children were regularly followed by FPs within the Pedianet network to ensure accurate exposure and outcome definitions, as previously described.[15] Cases of FPs enrolled in the Evolute study were excluded in the 2023-2024 comparison (ie, the season in which the Evolute FPs had available Ag-RDTs). All the VLRTI diagnoses were identified with *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)* codes and using the free-text field, as reported in previous work on the Pedianet database, and were cleaned using an infection duration algorithm to identify the primordial infectious event.[16]

Rapid Test Assessment

In cases in the main cohort, pediatricians collected a nasopharyngeal swab sample and immediately performed an Ag-RDT after obtaining informed consent signed by parents. The Ag-RDT used was a rapid antigen test (screen test SARS-CoV-2, influenza A+B, and RSV CE-marked in vitro diagnostic [IVD] rapid antigen test; REF: ISIR-535[SC-2399-20]; Hangzhou AllTest Biotech Co). According to the instructions for use (number 146555702) for the RSV CE-marked IVD rapid antigen test (April 6, 2023, revision), the declared sensitivity and specificity for RSV were 94.3% (95% CI, 80.8%-99.3%) and 96.2% (95% CI, 92.8%-98.2%), respectively.[17]

Exposure Definitions and Comparison

We defined 5 different exposure scenarios of interest with the appropriate reference group, as reported in **Table 1**: (1) RSV-positive vs RSV-negative cases (main cohort), (2) RSV-tested (either positive or negative) vs clinically diagnosed VLRTI cases, (3) RSV-positive vs clinically diagnosed VLRTI cases, (4) RSV-tested vs clinically diagnosed bronchiolitis cases in children younger than 24 months, and (5) RSV-positive vs clinically diagnosed bronchiolitis cases in children younger than 24 months. For scenarios 2 to 5, we used a 1:1 matched cohort design. Each exposed child was matched to an unexposed child based on age at diagnosis (in months), sex, and period of diagnosis (middle of the season [December-February] or extremes of the season [November, March, or April]). The index date was defined as the date of diagnosis. The success of matching was evaluated using standardized mean differences (SMDs), provided in eTable 1 in Supplement 1. Diagnoses of influenza and/or SARS-CoV-2 infection were excluded from the reference group. Because the main cohort included children who received the Ag-RDT and the comparison cases were matched to resemble them, our design estimated the average treatment effect on the treated (ATT). In other words, the outcome measures reflect how antibiotic prescribing differed for children who were tested compared with how the same children would have been treated without the test. For this reason, analyses were conducted only on the matched cohort.

Outcome Definition

The outcome of interest consisted of all the prescriptions referring to Anatomical Therapeutic Chemical (ATC) code J01* dispensed within 14 days after the index date. We used a 14-day follow-up period for consistency with clinical guidelines for treating respiratory tract infections. Prescriptions related to a concomitant diagnosis of bacterial infection (such as acute otitis media, community-acquired pneumonia, streptococcal pharyngitis, and urinary tract infections retrieved by *ICD-9-CM* codes and free-text string search) or dispensed after a positive C-reactive protein test performed in the exposure period were removed from the analysis. For each case, prescriptions were deduplicated by ATC code and prescription date.

Statistical Analysis

Baseline characteristics of the cohorts were summarized using appropriate descriptive statistics, including frequencies and percentages for categorical variables and medians with IQRs for continuous variables. Missing values for the Area Deprivation Index (ADI) were treated as a separate category because the underlying missingness mechanism was heterogenous and not adequately modeled using standard imputation approaches. Prescription rates expressed in 10 person-days (number of prescriptions every 10 days gained in the cohort) were calculated to describe the antibiotics prescription rate. Log-binomial models were used to estimate the relative risk (RR) and the 95% CI of receiving at least 1 antibiotic prescription, with the diagnosis episode as the statistical unit. Comparisons in scenario 1 were adjusted for sex, age, period of diagnosis, and ADI to account for socioeconomic disadvantage potentially affecting antibiotic use.[18] For scenarios 2 to 5, which relied on 1:1 matched cohorts, no postmatching adjustments were applied. Accordingly, unadjusted models

Table 1. Definition of Contrasts of Interest

Scenario[a]	Group: Exposure	Group: Reference
1. Main cohort	RSV-positive cases	RSV-negative cases
2. Main cohort vs VLRTI cohort	Tested VLRTIs (both RSV-positive and RSV-negative cases)	Clinically diagnosed VLRTI cases
3. RSV-VLRTI vs VLRTI cohort	RSV-positive VLRTI cases	Clinically diagnosed VLRTI cases
4. Main bronchiolitis vs bronchiolitis cohort	Tested bronchiolitis cases in patients aged <24 mo	Clinically diagnosed bronchiolitis cases in patients aged <24 mo
5. RSV-bronchiolitis vs bronchiolitis cohort	RSV-positive bronchiolitis cases in patients aged <24 mo	Clinically diagnosed bronchiolitis cases in patients aged <24 mo

Abbreviations: RSV, respiratory syncytial virus; VLRTI, viral lower respiratory tract infection.

[a] Comparisons in scenarios 2 to 5 were made in 2 different epidemiologic seasons, from November 2022 to April 2023 and November 2023 to April 2024.

were used in the matched samples to estimate the ATT. The use of the robust variance estimator to account for correlations within children with multiple diagnoses did not change the 95% CIs considerably in the unadjusted analyses; thus, correlation structures were omitted from all analyses. All the analyses were made according to the comparisons described in Table 1.

Several sensitivity analyses were performed to assess the robustness of our main findings. Analyses in scenario 2 were also performed after restricting the cohort to only cases of children aged less than 24 months. Moreover, we compared each case that underwent Ag-RDT in the Evolute cohort, which also comprised influenza and SARS-CoV-2 infection cases, with a clinically diagnosed VLRTI case. Furthermore, although matching may reduce confounding by ADI to the extent that age, sex, and period of diagnosis capture overlapping information, we additionally adjusted all models for ADI. In addition, to assess short-term clinical deterioration as a balancing measure, sensitivity analyses were conducted among children who did not receive an antibiotic prescription, comparing rates of emergency department visits or hospitalization within 14 days between children with a positive vs negative RSV test result. All statistical analyses were performed using SAS software, version 9.4 (SAS Institute Inc).

Results

Main Cohort

A total of 281 cases were enrolled in the Evolute study. Of these, 25 were excluded because they were positive for influenza or SARS-CoV-2 or had dubious results. A total of 256 VLRTI episodes were included in the main cohort (median age, 15.06 months [IQR, 11.61-22.72 months]; 123 females [48.05%] and 133 males [51.95%]) (**Table 2** and eFigure 1 in Supplement 1). Of these, 79 (30.86%) tested positive for RSV (hereafter, “RSV positive”), while 177 (69.14%) had a negative result for all tested viruses (hereafter, “RSV negative”). The study population was balanced in terms of age and sex, although RSV-negative cases were slightly younger than RSV-positive ones (median age, 14.95 months [IQR, 11.66-22.67 months] vs 15.34 months [IQR, 11.40-23.10 months], respectively), and there was a higher proportion of females among RSV-positive than RSV-negative cases (41 [51.90%] vs 82 [46.33%]). Most cases were from less deprived areas, with a decreasing prevalence trend across ADI quintiles from least deprived (58 of 238 [24.37%]) to most deprived (33 of 238 [13.87%]).

Table 2. Sociodemographic Characteristics of Cases Positive or Negative for RSV

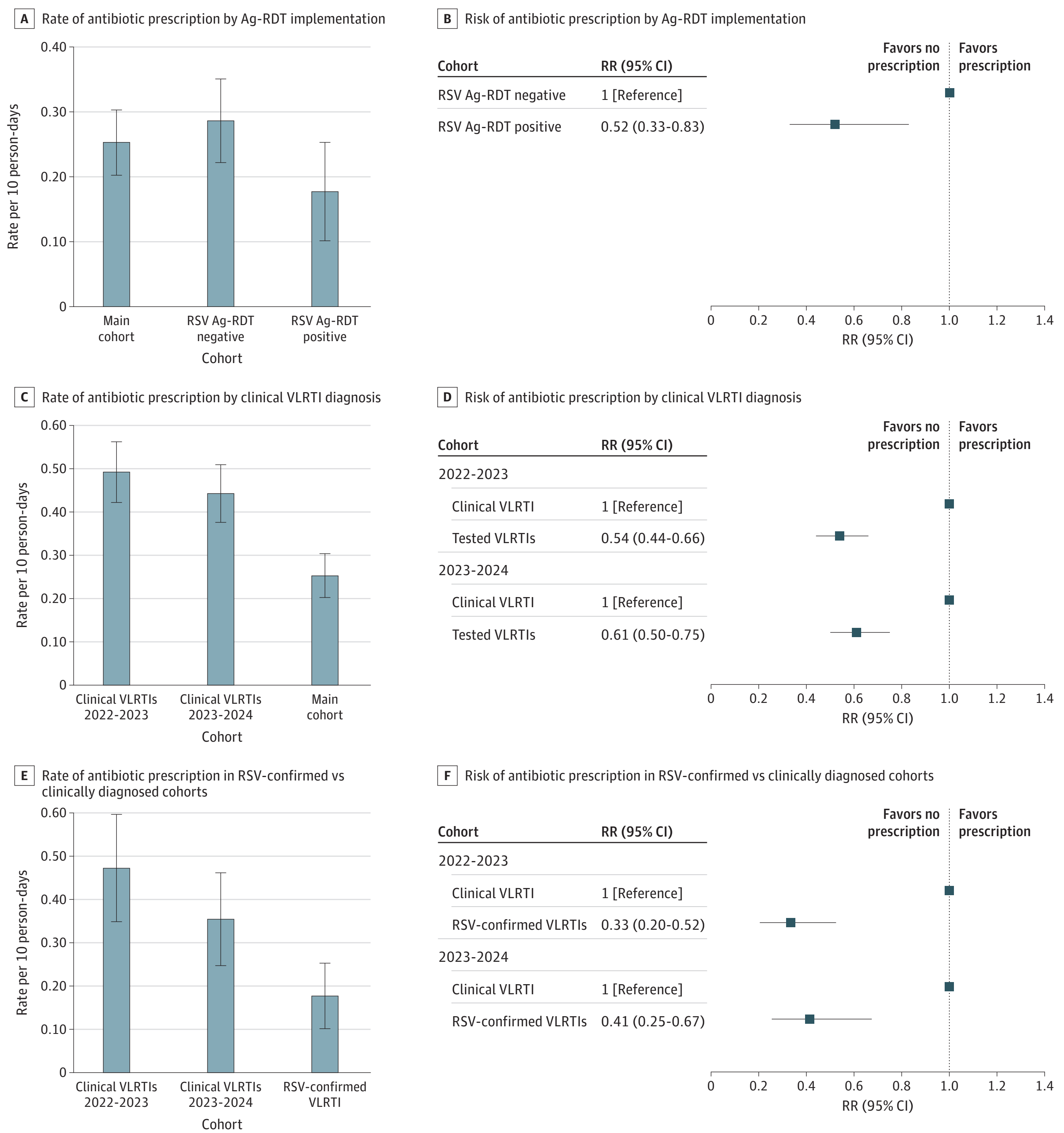
Characteristic	Cases, No. (%) Overall (N = 256)	RSV negative (n = 177)	RSV positive (n = 79)	SMD
Age at the test, mo				
Median (IQR)	15.06 (11.61-22.72)	14.95 (11.66-22.67)	15.34 (11.40-23.10)	0.0119
0 to <12	72 (28.13)	49 (27.68)	23 (29.11)	0.1286
12 to <16	65 (25.39)	48 (27.12)	17 (21.52)	
16 to <22	51 (19.92)	35 (19.77)	16 (20.25)	
≥22	68 (26.56)	45 (25.42)	23 (29.11)	
Sex				
Female	123 (48.05)	82 (46.33)	41 (51.90)	0.1116
Male	133 (51.95)	95 (53.67)	38 (48.10)	
Area Deprivation Index				
Quintile, No./total No. (%)				
1 (Least deprived)	58/238 (24.37)	39/162 (24.07)	19/76 (25.00)	0.2527
2	61/238 (25.63)	38/162 (23.46)	23/76 (30.26)	
3	44/238 (18.49)	32/162 (19.75)	12/76 (15.79)	
4	42/238 (17.65)	29/162 (17.90)	13/76 (17.11)	
5	33/238 (13.87)	24/162 (14.81)	9/76 (11.84)	
Missing data	18 (7.03)	15 (8.47)	3 (3.80)	

Abbreviations: RSV, respiratory syncytial virus; SMD, standardized mean difference.

Although not a statistically significant difference, RSV-positive cases had a higher cumulative percentage of nonsevere ADI (level 3 or lower) compared with RSV-negative cases (54 of 76 [71.05%] vs 109 of 162 [67.28%]) (Table 2).

Overall, antibiotic prescribing rates averaged 0.25 (95% CI, 0.20-0.30) prescriptions per 10 person-days. RSV-negative cases had higher antibiotic prescribing rates (0.29 [95% CI, 0.22-0.35] per 10 person-days) compared with positive cases (0.18 [95% CI, 0.10-0.25] per 10 person-days) (**Figure 1**A and eTable 2 in Supplement 1). Among RSV-positive cases, 16 (20.25%) received at least 1

Figure 1. Bar Graphs of Antibiotic Prescription Rates and Forest Plots Illustrating Risk of Receiving at Least 1 Antibiotic Prescription Within 14 Days of the Episode, by Detection of Infection



A, C, and E, whiskers indicate 95% CIs. Ag-RDT indicates antigen rapid diagnostic test; RR, relative risk; RSV, respiratory syncytial virus; VLRTI, viral lower respiratory tract infection.

antibiotic prescription, compared with 70 (39.55%) among RSV-negative cases. Detection of RSV (scenario 1) was associated with a reduction in the risk of receiving at least 1 antibiotic prescription within 14 days of the LRTI episode (RR, 0.52; 95% CI, 0.33-0.83) (Figure 1B and eTable 2 in Supplement 1).

Tested VLRTIs and RSV-Confirmed VLRTIs vs Clinically Diagnosed VLRTIs

Overall, RSV Ag-RDT implementation was associated with a reduction in the risk of antibiotic therapy in the cohort with any testing for VLRTIs compared with the matched cohort with clinically diagnosed VLRTIs (scenario 2) in the 2023-2024 (RR, 0.61; 95% CI, 0.50-0.75) and 2022-2023 (RR, 0.54; 95% CI, 0.44-0.66) seasons (Figure 1D and eTable 2 in Supplement 1). The outcome was even more pronounced when focusing specifically on RSV-confirmed VLRTIs: RSV confirmation was associated with a reduction in risk of antibiotic therapy compared with the matched clinically diagnosed cohort (scenario 3) in the 2023-2024 (RR, 0.41; 95% CI, 0.25-0.67) and 2022-2023 (RR, 0.33; 95% CI: 0.20-0.52) seasons (Figure 1F and eTable 2 in Supplement 1).

Tested Bronchiolitis and RSV-Confirmed Bronchiolitis vs Clinically Diagnosed Bronchiolitis Cohorts

When restricting the cohort to children under 24 months of age with a diagnosis of bronchiolitis, the impact of RSV Ag-RDT implementation remained evident, although statistical power was reduced in some comparisons. Specifically, the implementation was associated with a reduction in the risk of receiving at least 1 antibiotic prescription compared with clinically diagnosed bronchiolitis cases (scenario 4) in the 2022-2023 season (RR, 0.56; 95% CI, 0.33-0.95) but not in the 2023-2024 season (RR, 0.75; 95% CI, 0.42-1.33) (**Figure 2**B and eTable 2 in Supplement 1). The outcome was more pronounced when focusing on RSV-confirmed bronchiolitis, which was associated with reduced prescribing compared with a clinical bronchiolitis diagnosis (scenario 5) in the 2022-2023 season (RR, 0.33; 95% CI, 0.15-0.76) but not in the 2023-2024 season (RR, 0.43; 95% CI, 0.18-1.00) (Figure 2D and eTable 2 in Supplement 1). Sensitivity analyses supported the main finding (eTable 2 and eFigures 2 and 3 in Supplement 1), and demographic characteristics of the matched cohorts can be found in eTable 3 in Supplement 1. In addition, in sensitivity analyses among children who did not receive an antibiotic prescription, emergency department visits or hospitalizations within 14 days occurred in 10 of 107 RSV-negative cases (9.35%) and in 5 of 63 RSV-positive cases (7.94%), with no statistically significant difference between groups.

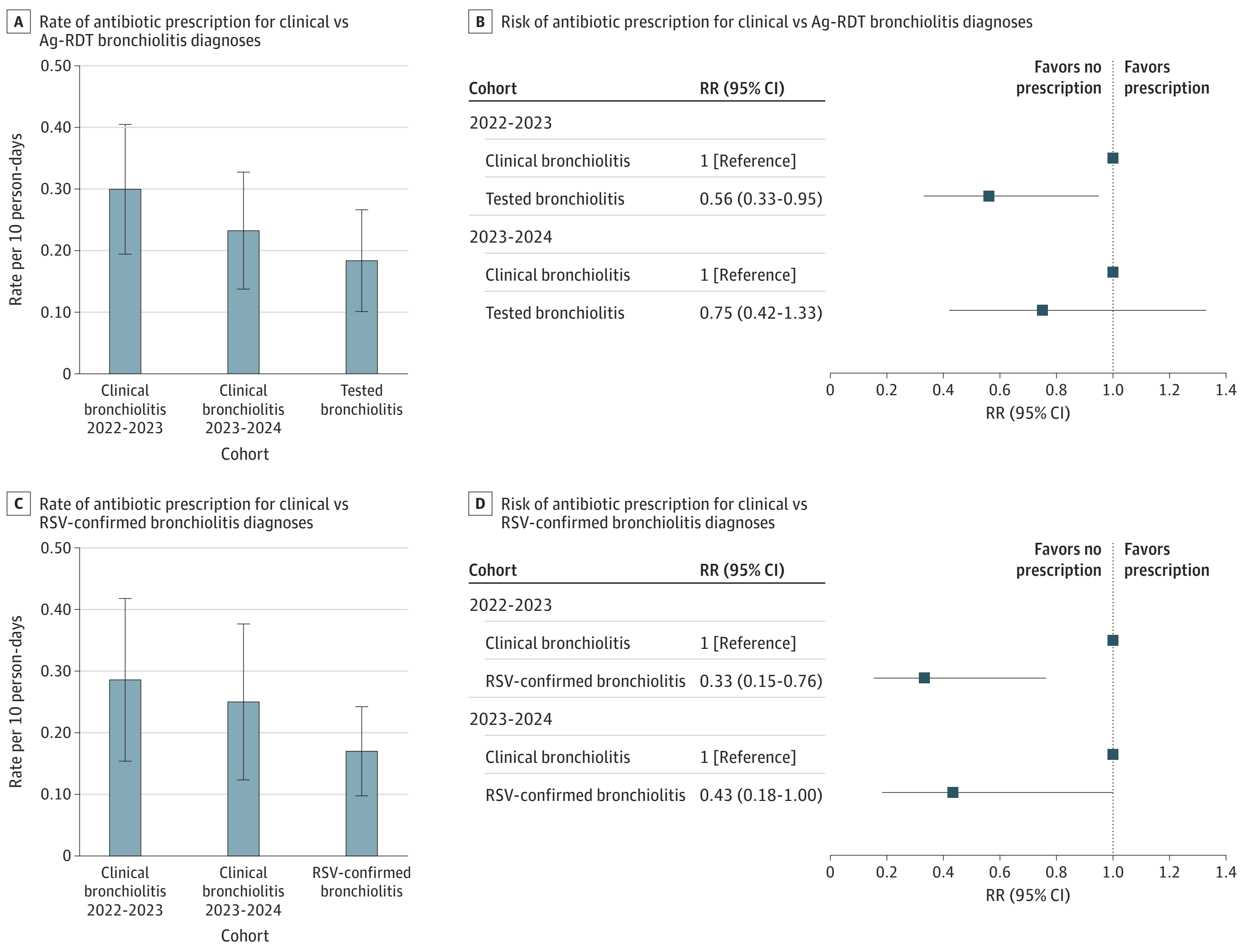
Discussion

To our knowledge, this is the first study to evaluate outpatient data on the association between implementing Ag-RDTs for RSV and reduction in antibiotic prescribing rates, specifically through comparisons with contemporaneous and historical cohorts with clinically diagnosed VLRTIs or bronchiolitis. This investigation addresses a critical gap in the existing literature and underscores the importance of accurate diagnostic tools in guiding clinical decision-making and promoting more appropriate antibiotic use.

These findings contrast with previous literature. Thibeault et al[19] found no significant difference in antibiotic prescribing between RSV-positive and RSV-negative hospitalized cases (10% vs 7% received intravenous antibiotics, respectively; $P = .61$). Thibeault et al[19] identified 2 key predictors of intravenous and oral antibiotic discontinuation in RSV-positive cases: age older than 3 months and the absence of pneumonia or otitis media. These findings may reflect clinicians' heightened concern about severe outcomes or bacterial coinfections in younger, more susceptible children. The discrepancy between that study and ours may be attributable to differences in study populations. While Thibeault and colleagues'[19] analysis included hospitalized children (likely representing more severe and complex cases), the present study focused exclusively on patients aged 9 to 36 months who were cared for in outpatient settings, excluding younger infants at increased risk for bacterial coinfection and incomplete immunization.

However, different studies have reported the overuse of antibiotics in older children with LRTIs caused by RSV without a concomitant bacterial coinfection,[20,21] highlighting a critical need to improve antibiotic prescribing practices. In a study by Van Houten et al,[20] the amount of antibiotic overuse in children with RSV infections was evaluated using an expert panel diagnosis. Of the 188 children with RSV-positive swab samples, 92 (49%) were treated with antibiotics, but only 27 (29%) had a bacterial coinfection, while 57 (62%) had no diagnosis of bacterial coinfection. Overuse and misuse of antibiotics are not only a community issue, as they contribute to the rise of resistance over time, but also an individual concern, since antibiotics, like all drugs, can cause adverse effects, potentially resulting in hospital admission. Consistent results were reported in 2021 by Barbieri et al[22] after the introduction of Italy's national bronchiolitis management recommendations. Their analysis focused on antibiotic prescriptions for children aged 0 to 24 months across 3 time frames: prior to the release of the recommendations (December 2012 to December 2014), during the transitional phase (December 2014 to December 2015), and following implementation (December 2015 to December 2018). Despite the dissemination of these recommendations, the overall rate of antibiotic prescriptions remained unchanged, with 31.6% of patients continuing to receive antibiotic prescriptions in the initial cohort.

Figure 2. Bar Graphs of Antibiotic Prescription Rates and Forest Plots Illustrating Risk of Receiving at Least 1 Antibiotic Prescription Within 14 Days of the Episode, by Bronchiolitis Diagnosis



A and C, whiskers indicate 95% CIs. Ag-RDT indicates antigen rapid diagnostic test; RR, relative risk; RSV, respiratory syncytial virus.

However, subsequent informational initiatives, including the Choosing Wisely campaign, supported by the Italian Federation of Family Paediatricians, led to significant progress.[23] This campaign emphasized clinician education and provided patient-friendly materials advocating for evidence-based care, encapsulated in the slogan "doing more does not mean doing better." As reflected in our study, antibiotic prescribing has improved over time, with declining rates suggesting a positive impact of ongoing stewardship and awareness campaigns. However, the integration of RSV Ag-RDTs into clinical practice was associated with a substantially greater reduction in antibiotic use, reaching 0.25 prescriptions per 10 person-days.

Although the recent introduction of universal RSV immunoprophylaxis is expected to influence RSV epidemiology, in Italy its use is currently limited to infants during their first RSV season. In this population, immunoprophylaxis has been associated with a 23.6% (95% CI, 3.8%-39.3%) relative reduction in antibiotic prescriptions.[24] However, in the absence of preventive options for older children, reductions in unnecessary antibiotic use among children older than 10 months may depend more heavily on diagnostic tools and antimicrobial stewardship interventions. Moreover, in children over 12 months of age, clinical presentation of RSV often diverges from classic bronchiolitis, further complicating the differentiation between viral and bacterial infections based solely on clinical evaluation. In this context, RSV Ag-RDT may serve as a valuable tool to assist clinicians in distinguishing viral from bacterial etiologies and in guiding more appropriate treatment decisions.

Recent advancements in RSV diagnostics have led to the development of rapid, cost-effective bedside antigen tests, with sensitivity and specificity comparable to polymerase chain reaction (PCR).[10] Yin et al[25] reported high diagnostic performance of Ag-RDTs for RSV, showing sensitivity of 83.3% (95% CI, 43.6%-97.0%) and specificity of 100% (95% CI, 98.7%-100%) compared with molecular diagnostics, thereby supporting their utility for viral identification in pediatric populations. While the effectiveness and feasibility of these tests have been well established in adults across both outpatient and inpatient settings, evidence in children, particularly in primary care, remains limited and warrants further investigation.[26,27]

The widespread implementation of RSV Ag-RDTs remains limited by several key challenges. First, variability in the diagnostic performance of commercially available tests may reduce clinician confidence and hinder widespread adoption. Second, the subjective interpretation of colorimetric results in lateral flow assays can affect diagnostic accuracy. Third, the cost of Ag-RDTs, especially in low-resource settings, may limit routine use despite their potential to reduce unnecessary antibiotic prescriptions and support more targeted clinical decision-making. Nevertheless, this study's findings underscore the importance of combining RSV prevention strategies, including universal immunoprophylaxis, with Ag-RDT implementation and broader antimicrobial stewardship efforts to enhance prescribing practices and help achieve national and international targets to combat antimicrobial resistance, such as a 20% reduction in human antibiotic consumption by 2030.[28,29]

Strengths and Limitations

Our study offers several strengths. The ability to compare RSV-positive and RSV-negative cases enabled a direct evaluation of the consequences of Ag-RDT implementation for antibiotic prescribing, demonstrating a significant reduction. Additionally, the use of primary care data spanning multiple epidemiologic seasons (2022-2023 and 2023-2024) enhances the generalizability and robustness of our findings.

Several limitations should also be acknowledged. First, the relatively small sample size limited our ability to apply random-effects models to account for potential variability in prescribing behaviors across FPs; to partially mitigate this, we used a matched historical cohort design. Second, we were unable to adjust for disease severity, which may have influenced antibiotic prescribing decisions. However, prescriptions in cases with confirmed severity based on elevated PCR markers, when available, or with concomitant bacterial infection were excluded from the analysis to reduce severity-related misclassification. Third, the test's sensitivity may be lower than the value reported by the manufacturer, potentially due to variations in how it was performed by FPs in a primary care setting. Fourth, although the study did not initially include a balancing measure to assess unintended consequences of withholding antibiotics, our sensitivity analysis showed similar rates of emergency department visits or hospitalization within 14 days among children not prescribed antibiotics, regardless of RSV test results, with no apparent evidence of short-term clinical deterioration.

Conclusions

This cohort study of 256 children highlighted the potential of RSV Ag-RDTs to reduce inappropriate antibiotic prescribing for LRTIs in pediatric community settings. By improving diagnostic accuracy at the point of care, Ag-RDTs can support more targeted treatment decisions and strengthen antimicrobial stewardship. While these findings are promising, further large-scale research is warranted to confirm their generalizability and to assess the cost-effectiveness of Ag-RDT implementation as part of a broader strategy to optimize antibiotic use and combat antimicrobial resistance in children.

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SUPPLEMENT 1.

eAppendix. Evolute Study
eTable 1. Standardized Mean Differences for the Matching Procedures in the Different Contrasts of Interest
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SUPPLEMENT 2.

Nonauthor Collaborators

SUPPLEMENT 3.

Data Sharing Statement