RAPID PUBLIC HEALTH REPORT

RSV epidemiology in Primary Care in four Italian regions: A prospective multi-centre study in over 60-year-old adults across three winter seasons (2022 - 2023 - 2024)

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ABSTRACT

Background: Respiratory syncytial virus (RSV) is an under-recognised cause of acute respiratory infections (ARIs) in older adults, despite a burden comparable to influenza and the recent availability of RSV vaccines. Robust community-based data from Italian primary care are lacking.

Methods: We conducted a prospective, multicentre cohort study in four Italian regions (Liguria, Lombardy, Tuscany, Apulia) over three consecutive winter seasons (2022–2025). Community-dwelling adults ≥60 years presenting to participating general practitioners (GPs) with a WHO-defined ARI were enrolled. Nasopharyngeal swabs were collected and tested using a multiplex RT-PCR respiratory panel. RSV-positive participants were followed by telephone at day 14 (T14) and day 30 (T30). Adjusted prevalence ratios (PRs) for symptoms were estimated with Poisson regression.

Results: Among 664 ARI episodes, 663 had a valid RSV result, and 88 were RSV-positive (13.3%). Positivity rates varied by season (21.7% in 2022–23, 11.9% in 2023–24, and 10.4% in 2024–25) and region (range: 11.2–28.3%), with peaks occurring between ISO weeks 51 and 10. The median age of RSV-positive patients was 75 years (IQR,

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68–82); 42% were male. Compared with RSV-negative ARIs, RSV-positive cases had higher adjusted prevalence of cough (PR 1.07, 95% CI 1.02–1.13) and wheezing (PR 1.83, 95% CI 1.14–2.93); other symptoms overlapped substantially. RSV-B predominated (68.2%). Any co-infection occurred in 35.2% of RSV-positive cases, mainly with Haemophilus influenzae and Streptococcus pneumoniae. Median illness duration was 19.5 days (IQR 11.3–30.0). Within 14 days, 65.9% re-contacted their GP and 10.6% sought additional medical care; emergency visits (3.5%) and hospitalisations (2.4%) were uncommon.

Conclusions: Across three winters, RSV accounted for approximately one in eight medically attended ARIs in Italian adults ≥60 years, with prolonged illness also leading to hospitalisations and frequent re-consultations. These findings provide baseline data to support adult RSV vaccination policies and integration of RSV into routine respiratory surveillance in Italy.

Background

Respiratory syncytial virus (RSV) is a major cause of acute respiratory infections (ARIs) in adults aged 60 years and older, with a community burden and clinical severity that, in some seasons, equals that of influenza (1). In European countries, RSV is responsible for approximately 4–8% of symptomatic winter ARIs among community-dwelling older adults, with substantial heterogeneity by season, setting, and case definition adopted (2,3). Despite this burden, routine RSV testing among adults in primary care remains limited, as surveillance has traditionally focused on pediatric cases and hospital settings, resulting in under-detection in older adults (4–6). Initial symptoms of RSV infections in older adults are often nonspecific (such as cough, rhinorrhea, nasal congestion, and fatigue) and may not prompt patients to seek timely medical care (7). Moreover, healthcare providers (HCPs) frequently underestimate the severity of RSV. Additionally, currently available diagnostic tests, particularly antigen-based assays, exhibit low sensitivity in this age group. Suboptimal sampling methodologies and inappropriate timing of specimen collection further reduce diagnostic accuracy (8–10). A survey conducted in the United States showed that 61% of HCPs did not test for RSV due to the lack of specific treatments, while 57% rarely considered RSV a relevant pathogen. Collectively, these factors contribute to a substantial under-recognition of the RSV disease burden in adults, with significant implications for epidemiological surveillance and the planning of preventive interventions (11). Co-detection of bacterial pathogens (e.g., Streptococcus pneumoniae, Haemophilus influenzae) or concomitant respiratory viruses occurs in a subset of patients, with significant clinical relevance due to its association with increased disease severity (12,13).

Prevention options for older adults have recently expanded. In 2023, the European Medicines Agency (EMA) authorised two protein-based vaccines, RSVPreF3 (Arexvy, GSK) and bivalent RSVpreF (Abrysvo, Pfizer), followed by an mRNA vaccine (mResvia, Moderna) for older adults in 2024 (3,14,15). In Phase III trials, these vaccines reduced RSV-associated lower respiratory tract disease (LRTD) in adults aged 60 years or older during the first post-vaccination season (16). At the EU level, regulatory approval does not automatically translate into uniform national recommendations; implementation is progressing heterogeneously across Member States (17). In Italy, a 2024 Ministry of Health circular acknowledged the availability of adult RSV vaccines and emphasized general respiratory hygiene measures while national recommendations are being updated (17,18). Independent scientific-society guidance (Calendario per la Vita) has proposed prioritizing vaccination in individuals aged 75 years or older and in adults aged 60–74 years with chronic conditions, pending formal national inclusion (19). Within this evolving prevention landscape, community-based estimates from primary care are crucial for informing vaccine policy,

timing, and future impact evaluations. RSVComNet Italy previously reported the pediatric primary-care burden across multiple seasons and piloted an adult protocol in 2022–2023 (20–22). Building on the shared multicentre protocol used across the network, we here describe three consecutive winter seasons (2022–2025) of prospective surveillance in adults ≥60 years in Italian primary care, quantifying RSV positivity among ARI cases seeking medical attention, characterizing clinical presentation and co-detection of other pathogens at enrolment, and describing 30-day clinical course and healthcare utilization among RSV-positive cases.

Methods

We conducted a prospective, multicentre cohort study embedded in routine primary care across four Italian regions (Liguria, Lombardy, Tuscany, and Apulia) over three consecutive winter seasons (2022–2023, 2023–2024, and 2024–2025) as reported in Table 1. The study followed the RSVComNet protocol and Case Reporting Forms (CRFs) used by the network, harmonized locally for Italy. Enrolment windows were aligned with expected RSV circulation weeks and could be advanced or extended in response to local epidemiology, as pre-specified in the protocol. Community-dwelling adults aged 60 years or older who presented to participating general practitioners (GPs) with an acute respiratory infection (ARI) according to the case definition were enrolled by convenience sampling. The WHO community ARI case definition was used, which requires an acute onset of disease (≤10 days) plus at least one of the following signs and symptoms: cough, sore throat, shortness of breath, wheeze, or coryza.

Table 1. Study sites, recruitment periods, and participating pediatricians across seasons.

Season	2022-2023	2023-2024	2024-2025
Study period (weeks)	W48 - W13[b]	W44 - W15[b]	W46 - W19[b]
Region			
Puglia	participating	participating	participating
Toscana	coordinating	coordinating	coordinating
Liguria	participating	participating	participating
Lombardia	-	participating	participating
Total population (age ≥ 60 years)[a]	2.973.834	6.075.258	6.194.825
Availability of online platform	-	available	available

[a] Refers to the resident population in participating sites as of 1st of January, included in the study period. Data are publicly available and retrieved from the ISTAT database (accessed 07-11-2025). [b] Dates are expressed as ISO-8601 calendar weeks (Monday–Sunday).

At enrolment (T0), GPs recorded demographics, comorbidities, and symptoms in a standardized eCRF and collected a nasopharyngeal swab. Respiratory samples were collected and tested with the Allplex™ Respiratory Full Panel Assay (Seegene) to detect RSV positivity and other respiratory pathogens (viral and bacterial). Cycle thresholds (CTs) were not used for clinical inference. All swabs were processed at reference laboratories using multiplex real-time RT-PCR. RSV-positive participants were re-contacted at day 14 (T14) and day 30 (T30) using a structured questionnaire covering symptom persistence, medication use, healthcare utilization, and complications. The primary outcomes were the proportion of ARI episodes RSV-positive per season, illness duration among RSV-positive cases, defined as days from symptom onset to self-reported recovery (T14/T30 follow-up). Secondary outcomes included: symptom profile at T0; co-detections at T0; healthcare utilization within 30 days (repeat GP contacts, defined a priori as ≥2 consultations for the same illness; emergency department [ED] visit; hospitalization); and distribution of RSV subtypes. Data were entered into a secure web platform with role-based access and an audit trail.

Statistical analysis

Baseline characteristics were described as medians with IQRs (for continuous variables) and counts with percentages (for categorical variables). Proportions were reported with 95% confidence intervals. RSV positivity among ARI episodes was reported overall and stratified by season (2022–23; 2023–24; 2024–25) and by region. To compare symptom prevalence between RSV-positive

and RSV-negative ARIs at enrolment (T0), we estimated adjusted prevalence ratios (PRs) using Poisson regression. Models adjusted for age group (60–69, 70–79, 80–89, ≥90), sex, and season. Symptom variables recorded only from 2023–24 onwards (e.g., wheeze, muscle pain, headache) were analyzed with their available denominators as reported. The time distribution of cases was described using weekly (ISO week) positivity curves and the week of peak positivity per season. No formal time-series modeling was attempted, as recruitment intensity varied by site and season. A complete-case analysis for each endpoint was performed if missing levels were under 5%. Variables not collected in all seasons are shown with explicit denominators.

Ethics

All participants provided written informed consent for testing and for follow-up interviews. The study was conducted in accordance with the Declaration of Helsinki and the European GDPR. Ethics approvals were obtained in each season prior to enrolment, specifically:

- Season 2021-2022: the study was approved by the Medical Ethical Committee of OPBG Medical Centre (prot. 644_OPBG_2022 on 16/05/2022)
- Season 2022-2023: the study was approved by the Ethical Committee "Comitato Etico di Area Vasta Nord Ovest (CEAVNO) per la Sperimentazione clinica" of the Tuscany Region, Italy (prot. 22871_Dini on 25/10/2022).
- Season 2023-2024: the study was approved by the Ethical Committee "Comitato Etico di Area Vasta Nord Ovest (CEAVNO) per la Sperimentazione clinica" of the Tuscany Region, Italy (prot. 22871_Dini on 05/10/2023).

Results

Across three consecutive winter seasons (2022–23 to 2024–25), 664 subjects meeting the ARI case definition were enrolled from four Italian regions (Table 2). A valid RSV result was available for 663 of 664 (99.8%). Overall, 88/663 cases were RSV-positive (13.3%). During follow-up, 3 participants were lost at T14 (3/88; 3.4%), and another two were lost at T30 (2/85; 2.3%). Numbers of individuals at each stage of study are available in Figure 1. RSV positivity rate varied across seasons: 33/152 (21.7%) in 2022–23, 15/126 (11.9%) in 2023–24, and 40/385 (10.4%) in 2024–25. Regionally, positivity was 13.3% in Tuscany (26/196), 11.8% in Liguria (35/296), 11.2% in Lombardy (14/125), and 28.3% in Apulia (13/46). Weekly RSV positivity peaked at ISO week 51 in 2022–23 (positivity 0.62), week 9 in 2023–24 (0.50), and week 10 in 2024–25 (0.33), consistent with mid-winter activity across seasons. Among RSV-positive participants (n=88), median age was 75 years (IQR 68–82), and 37/88 (42%) were male; full characteristics are described in Table 2. RSV positivity was 11.6% in adults aged 60–69 years (25/215), 12.5% in those aged 70–79 years (34/271), 15.4% in those aged 80–89 years (24/156), and 21.7% in those aged ≥90 years (5/23).

Symptoms at presentation (T0)

In the whole ARI cohort, the most frequent symptoms were cough (91.6%), coryza (69.5%), fatigue (59.6%), sore throat (44.6%), fever (31.7%), dyspnea (28.4%), and wheezing (17.2%). Compared with RSV-negative ARIs, RSV-positive cases more often reported cough (96.6% vs 90.8%) and coryza (77.3% vs 68.3%); wheeze was notably higher in RSV-positive (29.1% vs 15.8%), whereas sore throat (39.8% vs 45.4%) and fatigue (53.4% vs 60.5%) were less frequent. Full results stratified by RSV positivity are available in Table 2. Adjusted prevalence ratios confirmed enrichment of cough (PR 1.07, 95% CI 1.02–1.13) and wheezing (PR 1.83, 95% CI 1.14–2.93) in RSV-positive vs RSV-negative ARIs; whereas the associations for coryza (PR 1.10, 95% CI 0.97–1.26), fever (PR 1.15, 95% CI 0.84–1.57), dyspnea (PR 1.06, 95% CI 0.75–1.50), sore throat (PR 0.88, 95% CI 0.67–1.15) and fatigue (PR 0.90, 95% CI 0.73–1.10) were not statistically significant.

Laboratory findings and co-infections

Overall, RSV subtype B was more common (60/88, 68.2%); while RSV-A accounted for 27/88 cases (30.7%); with one mixed case (1.1%). Any

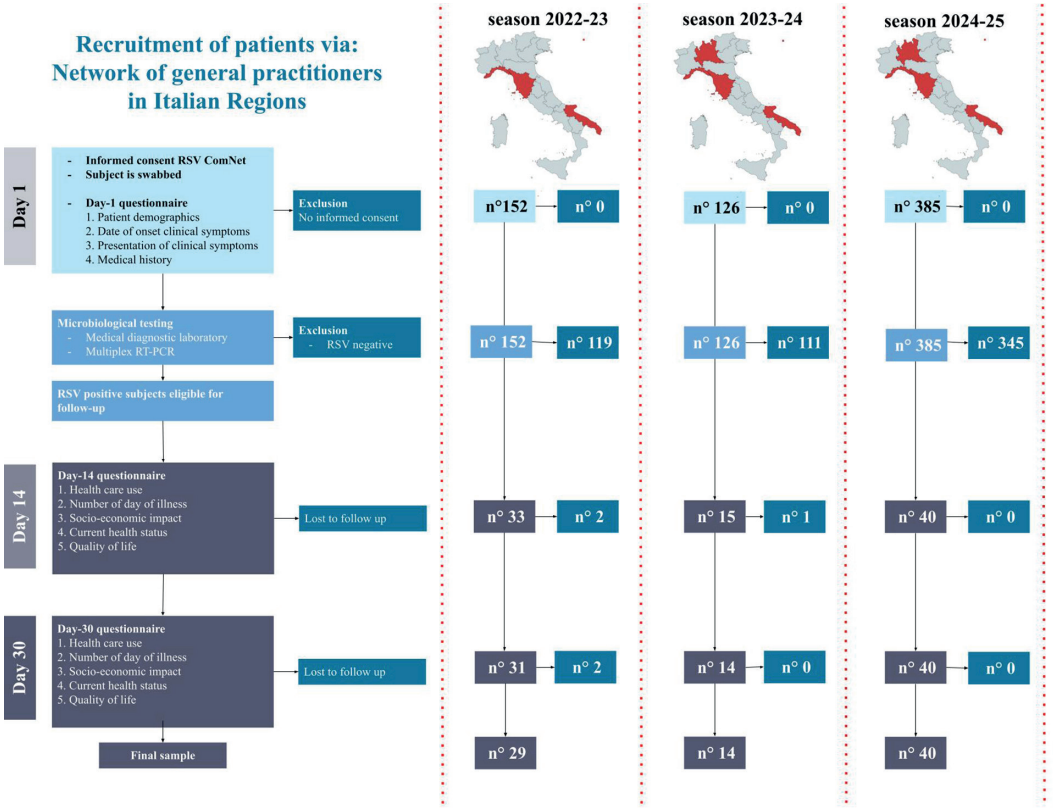

Figure 1. Flow diagram of participant enrollment and follow-up across study seasons.

co-infection was detected in 31/88 RSV cases (35.2%). Most commonly, *Haemophilus influenzae* in 16/31 (51.6%), *Streptococcus pneumoniae* in 4/31 (12.9%), rhinovirus in 4/31 (12.9%), influenza virus in 2/31 (6.4%), and SARS-CoV-2 in 2/31 (6.4%).

Clinical course and healthcare utilization (RSV-positive cohort)

At T14, 57/85 (67.1%) patients still presented symptoms, with 0/85 (0%) still reporting fever, 5/85 (5.9%) dyspnea, 0/85 (0%) wheezing, 48/85 (56.5%) cough, 17/85 (20.0%) coryza, 4/85 (4.7%) sore throat, 1/85 (1.2%) feeding difficulties, 1/85 (1.2%) dehydration, 1/54 (1.9%) headache, and 0/54 (0%) muscle pain. The average number of symptoms at T14 was above 1 (1.12), with a range of 0 to 6 (median: 1, IQR: 1-2). At T30, 25/83 (30.1%) subjects still reported symptoms, with 1/83 (1.2%) still presenting fever, 2/83 (2.4%) dyspnea, 0/83 (0%) wheezing, 17/83 (20.5%) cough, 2/83 (2.4%) coryza, 1/83 (1.2%) sore throat, 0/83 (0%) feeding difficulties, 0/83 (0%) dehydration, 0/54 (0%) headache, and 0/54 (0%) muscle pain. The average number of reported symptoms at T30 was 0.36 with a range of 0 to 3 (median: 0, IQR: 0-1). The average symptom duration was 20.6 days, with a range of 2-39 days (median: 19.5, IQR: 11.25 -30). Among the RSV-positive cohort, 56/85 (65.9%) patients contacted their family physician within 14 days of the swab collection date, and 9/85 (10.6%) patients contacted other medical professionals within the same time frame. Furthermore, 3/85 (3.5%) patients accessed the ER from T0 to T14, and 2/85 (2.4%) were hospitalized during the same time frame.

Discussion

Our study provides the first multicentre estimate of the burden of respiratory syncytial virus (RSV) among adults aged 60 years and older in Italian

Table 2. Baseline characteristics of enrolled subjects.

	Total	RSV positive	RSV negative
N	664	88	576
Season			
2022-2023	152 (23%)	33 (38%)	119 (21%)
2023-2024	126 (19%)	15 (17%)	111(19%)
2024-2025	386 (58%)	40 (45%)	346 (60%)
Region			
Puglia	46 (7%)	13 (15%)	33 (6%)
Toscana	196 (30%)	26 (30%)	170 (30%)
Liguria	296 (45%)	35 (40%)	261 (45%)
Lombardia	126 (19%)	14 (16%)	112 (19%)
Demographics			
Median Age in months (IQR)	74 (67-80)	75 (68-82)	74 (67 - 80)
Age category (years)			
60 – 69	215 (32%)	25 (28%)	189 (33%)
70 – 79	271 (41%)	34 (39%)	237 (41%)
80 – 89	156 (24%)	24 (27%)	132 (23%)
> 89	23 (3%)	5 (6%)	18 (3%)
Males	278 (42%)	37 (42%)	241(42%)
Symptoms at T0			
Fever	210 (32%)	31 (35%)	179 (31%)
Cough	607 (92%)	85 (97%)	522 (91%)
Coryza	461 (70%)	68 (77%)	393 (69%)
Wheezing	88/545 (16%)*	16/55 (29%)*	72/457 (16%)*
Dyspnea	188 (28%)	27 (31%)	162 (28%)
Sore throat	296 (45%)	40 (45%)	261 (45%)
Feeding difficulty	133 (20%)	14 (16%)	119 (21%)
Dehydration	24 (4%)	2 (2%)	22 (3%)
Fatigue	395 (60%)	47 (53%)	348 (60%)
Muscle pain	190/545 (35%)*	18/55 (33%)*	172/457 (38%)*
Headache	155/545 (28%)*	17/55 (31%)*	138/457 (30%)*
Laboratory results			
RSV	88/663 (13%)	n/a	n/a
A	n/a	27 (31%)	n/a
B	n/a	60 (69%)	n/a
A & B	n/a	1 (1%)	n/a
Other respiratory virus	362 (55%)	15 (17%)	347 (60%)
Influenza[a]	88 (13%)	2 (2%)	86 (15%)
Sars-CoV-2[a]	48 (7%)	2 (2%)	46 (8%)
Other[a]	257 (39%)	13 (15%)	244 (42%)
Bacterial Coinfection	176 (27%)	18 (20%)	158 (27%)
Negative swab	72 (11%)	n/a	72 (13%)

All reported as n/N (%), unless indicated otherwise. *Abbreviations:* n/a: not applicable.

primary care. Across four regions and three consecutive winters (2022–2025), RSV accounted for 13% of acute respiratory infections (ARIs), a proportion consistent with systematic reviews that report RSV may account for up to 12% of medically attended ARIs in older adults (23). Our findings confirm that RSV represents a substantial contributor to the clinical impact of winter respiratory diseases in the Italian elderly population, comparable in magnitude to that historically attributed to influenza (24). RSV positivity varied between 10% and 22% across seasons, reflecting the well-described variability in RSV activity during different seasons. The timing of peak detection, spanning ISO weeks 51–10, aligns with winter circulation patterns observed across Europe (25). The clinical picture of RSV-positive adults was dominated by cough, coryza, and fatigue, as previously reported (26). Notably, wheezing was reported at T0 almost twice as often in RSV-positive compared with RSV-negative ARIs (29% vs 16%). Yet emergency department visits and hospitalisations remained limited, with the majority of episodes managed by general practitioners. This finding emphasizes the distinct clinical presentations of ARI by etiological agent. A similar study from a community cohort in the U.S. reported higher odds of wheezing in RSV-positive compared with RSV-negative, but with considerable symptom overlap and without a clear ability to discriminate severe from non-severe infections, underscoring the need for molecular testing to guide the clinical management of the case (27). The duration of symptoms in our cohort was longer than that reported in other studies, with an average of 20.6 days (IQR, 11-30) and 30% symptom persistence at the 30-day follow-up. In a large European community-based cohort of older adults (RESCEU), PCR-confirmed RSV ARI had an average duration of approximately 19 days (IQR 13-27), and 22% of patients were still symptomatic at day 28 (28). The age distribution may partially explain this difference; our Italian cohort included a higher proportion of participants aged ≥75 years and community-dwelling adults, closely followed by family practitioners, whereas the RESCEU cohort was generally healthier. Nearly two-thirds of RSV-positive participants re-contacted their general practitioner within two weeks, and 10% sought additional medical advice, suggesting a sustained clinical and administrative workload for primary care. This pattern parallels previous findings from Italy and other European countries showing that outpatient RSV disease, while rarely life-threatening, generates a large cumulative burden because of its high frequency and extended course (28). A peculiarity of our cohort is the high proportion of co-detections (17%), primarily with *Haemophilus influenzae* and *Streptococcus pneumoniae*. These rates may reflect the systematic use of a multiplex PCR panel across all sites and the high prevalence of chronic airway colonization among older adults, particularly those with chronic airway disease. Their detection in nasopharyngeal samples does not, by itself, establish a causal role in the acute illness.

This study has several strengths. It is, to our knowledge, the first multicentre Italian surveillance study of RSV among adults aged 60 years or older, implemented prospectively and over three full seasons, using harmonized definitions and laboratory methods. The use of the same protocol and case definition, including laboratory testing with a PCR multiplex test at all sites, ensured comparability and enabled analysis of co-pathogens. Meanwhile, structured 14 and 30-day follow-ups captured the clinical trajectory and healthcare utilization beyond the initial consultation. These baseline data are valuable for future policy planning, particularly given that RSV vaccination has not yet been introduced in Italy (29). However, some limitations should be acknowledged. Participants represent community-dwelling older adults consulting during office hours and recruited via convenience sampling; as a consequence, patients with more severe ARIs requiring urgent care might have been excluded, leading to loss of valuable data. RSV positivity rates vary among regions due to different volumes of patients recruited; a smaller sample could lead to higher positivity rates caused by selection bias. Moreover, PCR testing is unable to distinguish between microbial co-infection and co-detection in nasopharyngeal samples, to establish the exact ARI etiology. Symptom reporting and recovery at T14 and T30 were self-assessed, which could introduce recall bias. Throughout the first season (2022-2023), the symptoms wheezing, muscle pain, and headache, were not collected as reported in Table 2. As follow-up was restricted to RSV-positive patients, comparative data with RSV-negative or influenza-positive cases could not be analysed within this cohort. Finally,

the absence of pre-illness quality-of-life measures limits the quantification of functional decline. Participation of GPs in RSVComNet was voluntary and independent of their involvement in the national Respivirnet surveillance. Participation in Respivirnet was neither an inclusion nor an exclusion criterion; therefore, some overlap among participating GPs is possible, although this information was not collected.

Conclusions

In conclusion, RSV accounted for one in eight medically attended acute respiratory infections (ARIs) among Italian adults aged ≥60 years, also leading to hospitalisations during three consecutive winter seasons, confirming that RSV represents a major cause of respiratory morbidity in the community setting. Illness was typically prolonged, lasting nearly three weeks on average, and resulted in frequent re-consultations with general practitioners. Although the relatively small number of subjects followed up, some hospitalizations were reported, indicating the presence of severe cases even in the primary care setting. Moreover, the frequency of bacterial co-detection highlights the need for enhanced diagnostic awareness and rational prescribing of antibiotics. Overall, these findings provide baseline data for Italy at a pivotal time in the development of RSV prevention policies. As adult RSV vaccination becomes available, community-based surveillance, such as this, will be essential to guide prioritization, evaluate vaccine effectiveness, and support the integration of RSV monitoring into national respiratory disease surveillance systems.

Authors' Contributions: FB and CR conceived the paper. FB, FT, BC, MP, ALDA, and CR performed the literature search and drafted the manuscript. FB and FT performed the data extraction and analysis. All the authors provided expert insights, critically reviewed the drafts, and provided feedback. All the authors approved the final manuscript.

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