Vaccine effectiveness of a bivalent respiratory syncytial virus (RSV) pre-F vaccine against RSV-associated hospital admission among adults aged 75–79 years in England: a multicentre, test-negative, case–control study

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Summary

Background A respiratory syncytial virus (RSV) vaccination programme for older adults using bivalent pre-F vaccine was introduced in England from Sept 1, 2024. Although vaccine effectiveness has been reported against all-cause RSV-associated respiratory hospital admissions, data are scarce on vaccine effectiveness against different presentations of RSV-associated illness, such as exacerbation of chronic illness.

Methods This multicentre, test-negative, case–control study used data from a national, hospital-based, acute respiratory infection sentinel surveillance (HARISS) system across 14 hospitals in England. Eligibility criteria were vaccine-eligible adults aged 75–79 years admitted to hospital with acute respiratory infection (ARI) for ≥24 h and tested with molecular diagnostic assays within 48 h of admission. Cases were RSV positive, and controls were negative for RSV, influenza, and SARS-CoV-2. Vaccination status and data on sex were obtained from the National Immunisation Information System. The primary outcome was hospital admission due to RSV-associated ARI, which was tested for using nasopharyngeal or combined nose and throat swabs. Clinical data were collected using a structured questionnaire.

Findings Between Oct 1, 2024, and March 31, 2025, 1006 older adults were admitted to hospital with ARI; 173 were RSV positive (cases) and 833 were RSV negative (controls). 526 (52·3%) of 1006 individuals were female and 480 (47·7%) were male. Mean age was 77·8 years (SD 1·4) in individuals who were RSV positive and 77·6 years (SD 1·3) in those who were negative for RSV, influenza, and SARS-CoV-2. Vaccine effectiveness was 82·3% (95% CI 70·6–90·0) against hospitalisation for any RSV-associated ARI and 86·7% (75·4–93·6) in those with severe disease including oxygen supplementation. Vaccine effectiveness was 88·6% (75·6–95·6) among individuals admitted due to lower respiratory tract infection, including pneumonia, 77·4% (42·4–92·8) due to exacerbation of chronic lung disease, and 78·8% (47·8–93·0) due to exacerbation of chronic heart disease, lung disease, and/or frailty. In individuals with immunosuppression, vaccine effectiveness was 72·8% (39·5–89·3).

Interpretation This study provides evidence that the RSV pre-F vaccine is highly effective against RSV-associated hospital admissions, including exacerbations of chronic disease, and in adults with immunosuppression.

Funding UK Health Security Agency.

Introduction

Respiratory syncytial virus (RSV) is a common seasonal respiratory virus that is an important cause of acute respiratory infection in older adults (aged ≥65 years) in the UK, resulting in hospital admission and mortality.[1,2] Previous studies conducted in the UK have estimated an annual hospital admission rate of 71 per 100 000 people in adults aged 65–74 years, increasing to 251 per 100 000 in adults aged 75 years and older.[2] Those living with frailty and comorbidities, such as chronic obstructive pulmonary disease (COPD) and chronic heart disease, are at particularly high risk of severe clinical outcomes from RSV infection.[3–5] In a study in England during winter 2023–24, 22·6% of older adults admitted to hospital with RSV-associated acute respiratory infection were aged 75–79 years. A high proportion (84%) of these individuals had at least one comorbidity, and 29% had immunosuppression.[6]

From Sept 1, 2024, an RSV immunisation programme for older adults was introduced in England. The programme offers a single dose of bivalent RSV pre-F vaccine (Abrysvo, Pfizer, New York, NY, USA) to all adults turning 75 years old alongside a one-off catch-up campaign for those aged 75–79 years.[7] The overall vaccine coverage in the catch-up cohort in England reached 60·3% as of March 31, 2025.[8] Clinical

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Research in context

Evidence before this study

Respiratory syncytial virus (RSV) is a common seasonal respiratory virus causing acute respiratory infection (ARI) in older adults. Individuals with frailty and comorbidities are at high risk of severe clinical outcomes. An RSV vaccination programme for adults aged 75–79 years was introduced in England on Sept 1, 2024, offering a single dose of bivalent RSV pre-F vaccine (Abrysvo, Pfizer, New York, NY, USA). Clinical trials report the efficacy and safety of the RSV pre-F vaccine but are limited by power to assess the efficacy against severe outcomes. Older adults with comorbidities were under-represented, and individuals with immunosuppression were excluded. Therefore, vaccine effectiveness studies are required.

We searched PubMed from Jan 1, 2023, to May 29, 2025, with no language filters, using the search terms (("RSV") OR ("respiratory syncytial")) AND (("vaccine effectiveness") OR ("VE")) AND ("adult"). Five studies conducted in the USA were relevant and reported vaccine effectiveness of 75–89% against hospital admission (69·5–73% in immunocompromised cohorts). Effectiveness for the RSV pre-F vaccine was 73–89%. Data on vaccine effectiveness against different presentations of RSV-associated hospital admissions, such as exacerbations of chronic illness, are scarce. These exacerbations represent a large proportion of RSV-related hospital admissions. Therefore, assessing vaccine effectiveness against different reasons for hospital admission is important for understanding the overall impact of RSV vaccination programmes.

Added value of this study

In this study, we seek to expand the existing evidence base using data from a national, hospital-based ARI sentinel surveillance (HARISS) system in England to report on end of season vaccine effectiveness from the first year of vaccine introduction in the UK. To our knowledge, our findings are among the first to show RSV vaccine effectiveness against RSV-associated hospital admissions in older adults in Europe. This study reports high effectiveness of the RSV pre-F vaccine (Abrysvo) against hospital admissions due to RSV-associated ARI in adults (aged 75–79 years on Sept 1, 2024). Vaccine effectiveness of RSV vaccination against hospital admission for any RSV-associated ARI was 82·3% (95% CI 70·6–90·0). Vaccine effectiveness was 77–89% for different reasons for admission, including lower respiratory tract infection and exacerbations of chronic lung disease, providing new evidence for RSV vaccine effectiveness in adults admitted to hospital due to RSV-associated chronic illness exacerbations. Vaccine protection was also maintained across different comorbidity groups, including those with immunosuppression. These data are important to support cost-effectiveness evaluations, vaccine policy decisions, and promotion of high vaccine coverage.

Implications of all the available evidence

The substantial vaccine protection reported using data from HARISS in England aligns with vaccine effectiveness estimates from the USA. The high vaccine effectiveness across different RSV-related presentations and in individuals with comorbid illnesses in this study supports the promotion of high vaccine coverage to reduce RSV-associated illness in older adults.

trials report safety and efficacy against lower respiratory tract disease of the RSV pre-F vaccine across two seasons but are limited by power to assess efficacy against severe outcomes, such as hospitalisation and oxygen supplementation. Older adults with comorbidities were also under-represented in these trials, and individuals with immunocompromise were excluded.[9–11] Real-world data from the USA, where RSV vaccination was introduced in 2023, have shown substantial vaccine effectiveness (75–89%[12–16]) against RSV-associated hospitalisation. There is also early evidence of a population-level impact of RSV vaccination in the UK.[17,18] However, there are currently few studies assessing the individual-level effectiveness of RSV vaccine outside of the USA and in health-care systems similar to those in the UK.

Additionally, published studies do not report vaccine effectiveness against RSV-associated exacerbations of chronic illnesses such as lung disease or heart disease, which are common reasons for admission in older adults with RSV infection.[4,5] Such presentations form a major component of RSV burden in older adults. Therefore, understanding the effectiveness against different types of hospitalisations is important when assessing the overall impact of RSV vaccination programmes. Furthermore, evidence is scarce on the effectiveness of RSV vaccination in different clinical risk groups, including immunosuppressed patients. These data are important to support cost-effectiveness evaluations and vaccine policy decisions on vaccine eligible groups. In this study, we seek to expand the evidence base using data from a national, hospital-based acute respiratory infection sentinel surveillance (HARISS) system in England to report on end of season vaccine effectiveness from the first year of vaccine introduction in the UK. HARISS is an active surveillance system designed to collect detailed clinical data from hospital sites, enabling the assessment of vaccine effectiveness across a range of admission reasons.

This study aimed to estimate the effectiveness of RSV vaccination against hospital admission due to RSV-associated acute respiratory infection in England during the 2024–25 RSV season in vaccine-eligible adults aged 75–79 years on Sept 1, 2024. We assessed vaccine

effectiveness by severity of illness, reason for admission, and comorbidity status, including immunosuppression.

Methods

Study design

This multicentre, test-negative, case–control study[19,20] used data from the HARISS system across 14 sentinel National Health Service (NHS) acute hospitals in England. HARISS is an active, enhanced surveillance system introduced in England in 2023–24 and expanded during 2024–25 from seven to 14 hospital trust sites. Sites within the surveillance network include geographical representation across England (appendix p 2). Adults were included who presented to hospital from Oct 1, 2024, to March 31, 2025.

The UK Health Security Agency (UKHSA) Caldicott Advisory Panel and Research Ethics and Governance Group considered this study epidemiological surveillance and granted approval (CAP-2023-23 and NR0379).

Participants

Individuals were classified as vaccinated if an RSV vaccination was administered at least 14 days before hospital presentation, as part of the UK's RSV immunisation programme. Individuals who were vaccinated 0–13 days before hospital presentation were classified as partly vaccinated and excluded. Individuals were classified as unvaccinated if they had not received an RSV vaccination at the time of hospital presentation. The UK's RSV vaccination programme for older adults uses the bivalent Abrysvo pre-F vaccine (Pfizer, New York, NY, USA), containing RSV-A and RSV-B derived antigen.

Cases were defined as adults eligible for RSV vaccine on Sept 1, 2024 (aged 75–79 years), admitted to hospital for at least 24 h due to acute respiratory infection, and positive for RSV on molecular diagnostic testing of samples taken within 48 h of admission. Controls were defined as adults eligible for RSV vaccine on Sept 1, 2024 (aged 75–79 years), admitted to hospital for at least 24 h due to acute respiratory infection, and negative for RSV, influenza, and SARS-CoV-2 on molecular diagnostic testing of samples taken within 48 h of hospital admission. RSV vaccination status was not known to those selecting controls for inclusion. For every participant who tested positive for RSV identified by the HARISS sites, an eligible control aged 75–79 years was selected from the same epidemiological week. This method ensured controls were selected throughout the whole RSV season, with more controls selected during periods of high RSV activity in older adults. Cases and controls were not matched.

For individuals with two admissions for RSV, only the first admission for RSV was included. For individuals with multiple admissions for test-negative acute respiratory infection, one admission was randomly selected for inclusion. If an individual was admitted for RSV and test-negative acute respiratory infection, only the RSV-positive admission was included in the study. Individuals were excluded from the study if they were not identified in the UKHSA's Immunisation Information System registry.

Surveillance was done under Regulation 3 of The Health Service (Control of Patient Information) Regulations 2002 (UK legislation),[21] which allows for data collection for public health purposes without requiring individual informed patient consent.

Procedures

Clinical and laboratory data, including reason for admission (multiple reasons selected if applicable), date of presentation to hospital, respiratory virus testing results, and clinical outcomes during admission, were captured from patients' medical records using the Snap Survey platform (Snap Surveys; clinical data collection questionnaire in the appendix). Medical records were reviewed by trained staff employed at each site. Clinical outcomes were captured 30 days after sample date or at discharge, whichever was sooner.

See Online for appendix

For more on Snap Surveys see https://www.snapsurveys.com/

RSV vaccination events, as well as demographic variables and comorbidity status, were collected from the Immunisation Information System. The Immunisation Information System is an individual-level vaccination and denominator record system of individuals registered for primary care in England. Data are provided by NHS England, which collates demographic information from general practice and secondary care records with vaccine administration data.[22] Data are validated using central NHS systems and updated daily to account for newly registered individuals and new vaccination events. The Immunisation Information System includes a record of an individual's sex, date of birth, ethnicity (reported by the Office for National Statistics ethnic group[23]), postcode (from which the Index of Multiple Deprivation can be derived), and date of death when applicable.

Comorbidities, including immunosuppression, were identified using NHS Cohorting as a Service, developed for call–recall purposes to identify at-risk individuals requiring the influenza or COVID-19 vaccine[24,25] based on electronic health records.[26] Immunosuppression includes individuals with immunosuppression due to disease or treatment as defined in the UK's Immunisation Against Infectious Disease Green Book.[24,25] The full list of disease or treatment classified as immunosuppression is provided in the appendix (p 5).

Outcomes

The primary outcome was hospital admission due to RSV-associated acute respiratory infection. All HARISS sites were advised to test nasopharyngeal or combined nose and throat swabs for RSV, influenza (A and B), and SARS-CoV-2 in patients aged 65 years or older who were admitted to hospital for at least 24 h for symptomatic acute respiratory infection. Symptomatic acute respiratory infection was defined as the presence

of any respiratory symptoms or fever and presenting with the following suspected diagnoses on admission: pneumonia or pneumonitis; non-pneumonia lower respiratory tract infection or acute bronchitis; exacerbation of chronic lung disease such as COPD or asthma; exacerbation of chronic heart disease such as heart failure; exacerbation of frailty or poor mobility such as a fall; or acute respiratory infection with another reason for admission (clinical data collection questionnaire is provided in the appendix pp 6–7). These diagnoses were ascertained from clinical diagnosis and documentation in the clinical notes. More than one suspected diagnosis could be selected in the questionnaire, if applicable. Symptoms and signs of acute respiratory infection on admission, and reasons for admission by case and control status are in the appendix (p 3).

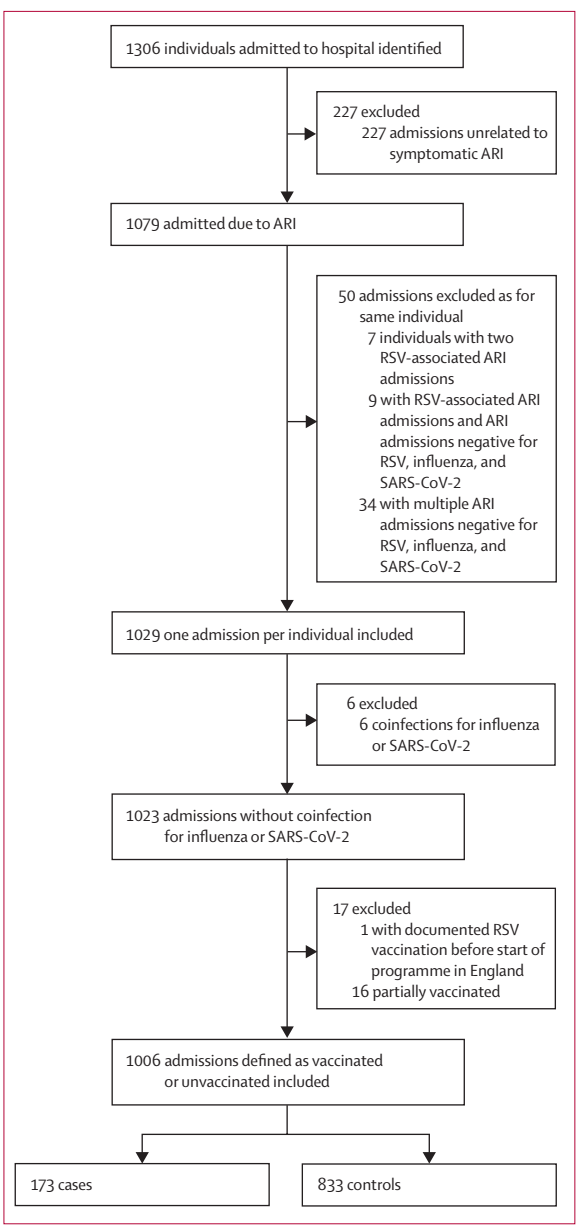

Figure 1: **Study flow diagram**
ARI=acute respiratory infection. RSV=respiratory syncytial virus.

Cases were excluded from the primary analysis if they had coinfection with influenza or SARS-CoV-2 to ensure that hospital admission was due to RSV-associated acute respiratory infection and not influenza or SARS-CoV-2, but they were included in a sensitivity analysis. Cases were excluded if they were not admitted to hospital due to acute respiratory infection.

Statistical analysis

To assess the effectiveness of RSV vaccination against hospital admission for RSV-associated acute respiratory infection, a test-negative, case–control analysis was conducted to compare the odds of vaccination among cases and controls using multivariable logistic regression. Vaccine effectiveness was calculated using vaccine effectiveness=1−odds ratio, with a 95% CI. The final multivariable logistic regression model was adjusted for days from start of the surveillance period to hospital presentation (using a cubic B-spline of degree 3), and presence of at least one comorbidity and/or immunosuppression. Other potential confounders examined for inclusion in the adjusted model were age, sex, ethnicity, Index of Multiple Deprivation, site, and region. These potential confounders did not change the vaccine effectiveness by 1% or more and were, therefore, not included in the final adjusted model, as per protocol. Potential confounders were identified using published literature from test-negative design studies on respiratory virus vaccine effectiveness[19,20] and have been outlined in the protocol.

Vaccine effectiveness was estimated among adults with severe disease, which was defined as the need during hospital admission of oxygen supplementation, high-flow nasal oxygen, non-invasive ventilation or continuous positive airway pressure, invasive ventilation or mechanical ventilation, and intensive care unit admission, as well as mortality within 30 days of hospital admission. Vaccine effectiveness was estimated according to the following reasons for hospital admission: lower respiratory tract infection including pneumonia; exacerbation of chronic lung disease (excluding lower respiratory tract infection); and exacerbation of chronic lung disease, heart disease, and/or frailty (excluding lower respiratory tract infection). Vaccine effectiveness was also stratified by comorbidity status: without immunosuppression; with immunosuppression; with chronic respiratory disease; and with chronic heart and vascular disease.

A sensitivity analysis was conducted to explore the inclusion of individuals that tested positive for influenza (A or B) and SARS-CoV-2 coinfection. A sensitivity analysis was also conducted to explore the inclusion of individuals who presented with at least one of the following symptoms or signs of acute respiratory infection on admission: fever,

hypothermia, new or increased cough, new or increased sputum volume or discolouration, new or increased shortness of breath, new or increased wheezing, and respiratory rate at least 25 breaths per min (appendix p 4). To reduce the inclusion of underpowered results, estimates of vaccine effectiveness were excluded if any expected cell count for vaccinated or unvaccinated cases or controls was less than 10.

Demographic characteristics and comorbidities were described for cases and controls and for vaccinated and unvaccinated. Mann-Whitney U tests, Pearson's Chi squared tests, and Fisher's exact tests, when applicable, were used to compare demographic and comorbidities characteristics between groups. p values less than 0·05 were regarded as statistically significant.

Missing data were minimised by using compulsory fields in the Snap Survey data collection tool. Individuals were included only if identified in the immunisation information system dataset. Missing data on ethnicity and Index of Multiple Deprivation have been reported and accounted for using the missing indicator approach. Analyses were completed using R version 4.3.2.

Role of the funding source

The UK Health Security Agency, which funded the HARISS surveillance system and participating HARISS sites for this surveillance work (including the data collection for this study), was involved in the study design, data analysis, data interpretation, and writing of the report.

Results

Between Oct 1, 2024, and March 31, 2025, 1006 individuals were admitted to hospital and included in the study (173 cases and 833 controls; figure 1). Peak RSV-positive admissions occurred during Nov 18–24, 2024, with the second highest during Dec 16–22, 2024 (figure 2). 526 (52·3%) of 1006 individuals were female and 480 (47·7%) were male. Mean age was 77·8 years (SD 1·4) in individuals who were RSV positive and 77·6 years (SD 1·3) in those who were negative for RSV, influenza, and SARS-CoV-2. Most individuals were White (155 [89·6%] of 173 cases and 740 [88·8%] of 833 controls). Most individuals had at least one medical comorbidity (157 [90·8%] and 770 [92·4%]). Immunosuppression was present in 47 (27·2%) cases and 244 (26·9%) controls (table 1).

Among all included admissions, 324 (32·2%) of 1006 adults had received an RSV vaccination 14 days or more before presenting to hospital with an acute respiratory infection, comprising 16 (9·2%) cases and 308 (37·0%) controls (table 1). The main difference in demographic characteristics between vaccinated and unvaccinated groups was sex: 153 (47·2%) of 324 individuals were female in the vaccinated group and 373 (54·7%) of 682 were female in the unvaccinated group (p=0·027; table 2).

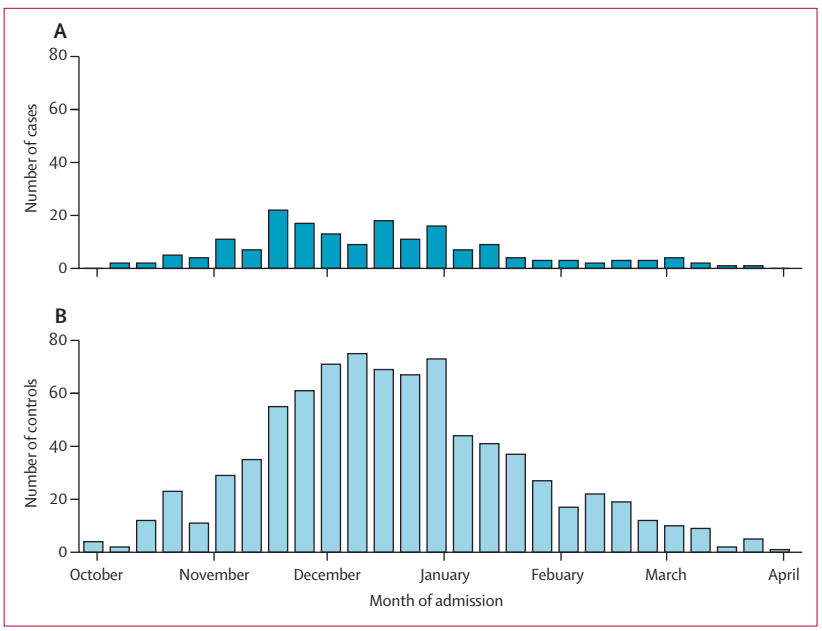

Figure 2: **Epidemiological curve of cases and controls by week of presentation to hospital**
Weekly counts of cases (A) and controls (B) between Oct 1, 2024, and March 31, 2025. Cases are RSV positive, and controls are negative for RSV, influenza, and SARS-CoV-2.

Among adults aged 75–79 years on Sept 1, 2024, the point estimate for effectiveness of RSV vaccination against hospital admission for any RSV-associated acute respiratory infection was 82·3% (95% CI 70·6–90·0). Vaccine effectiveness against any RSV-associated acute respiratory infection among those with severe disease was 86·7% (95% CI 75·4–93·6). Among individuals with severe disease, 560 (78·8%) of 711 received oxygen supplementation alone.

Vaccine effectiveness was 88·6% (95% CI 75·6–95·6) among individuals admitted to hospital due to a lower respiratory tract infection, including pneumonia; 77·4% (42·4–92·8) due to an exacerbation of chronic lung disease such as COPD; and 78·8% (47·8–93·0) due to an exacerbation of any chronic illness including chronic lung disease, chronic heart disease, and/or frailty (figure 3). When assessed according to underlying comorbid illnesses, vaccine effectiveness was 86·2% (95% CI 73·6–93·6) in individuals who were immunocompetent and 72·8% (39·5–89·3) in those with immunosuppression. Vaccine effectiveness was 77·0% (59·1–88·0) in individuals with chronic heart and vascular disease and 80·1% (62·4–90·6) in those with chronic respiratory disease (figure 3).

A sensitivity analysis including RSV-positive cases with influenza or SARS-CoV-2 coinfection (n=6) and a sensitivity analysis including individuals presenting with specific symptoms or signs of acute respiratory infection showed no meaningful changes in vaccine effectiveness against hospital admission due to RSV-associated acute respiratory infection (appendix p 4).

	Cases (n=173)	Controls (n=833)	p value
Age, years	77·8 (1·4)	77·6 (1·3)	0·13
Sex	..	..	0·67
Female	93 (53·8%)	433 (52·0%)	..
Male	80 (46·2%)	400 (48·0%)	..
Ethnicity	..	..	0·97
White	155 (89·6%)	740 (88·8%)	..
Asian or Asian British	6 (3·5%)	36 (4·3%)	..
Black, Black British, Caribbean, or African	1 (0·6%)	10 (1·2%)	..
Mixed or multiple ethnic groups	0	3 (0·4%)	..
Other	2 (1·2%)	12 (1·4%)	..
Missing	9 (5·2%)	32 (3·8%)	..
Index of Multiple Deprivation quintile*	..	..	0·35
1	41 (23·7%)	219 (26·3%)	..
2	22 (12·7%)	141 (16·9%)	..
3	36 (20·8%)	131 (15·7%)	..
4	36 (20·8%)	157 (18·8%)	..
5	37 (21·4%)	181 (21·7%)	..
Missing	1 (0·6%)	4 (0·5%)	..
Comorbidities			
At least one comorbidity	157 (90·8%)	770 (92·4%)	0·45
Chronic respiratory disease	93 (53·8%)	508 (61·0%)	0·078
Chronic neurological disease	48 (27·7%)	227 (27·3%)	0·89
Chronic liver disease	4 (2·3%)	25 (3·0%)	0·80
Chronic kidney disease	46 (26·6%)	213 (25·6%)	0·78
Chronic heart disease and vascular disease	110 (63·6%)	506 (60·7%)	0·49
Immunosuppression	47 (27·2%)	224 (26·9%)	0·94
Diabetes and other endocrine disorders	51 (29·5%)	242 (29·1%)	0·91
Morbid obesity	6 (3·5%)	42 (5·0%)	0·38
Severe mental illness	8 (4·6%)	25 (3·0%)	0·28
RSV vaccination status			
Vaccinated	16 (9·2%)	308 (37·0%)	<0·0001
Severe disease including oxygen use†	..	..	0·0039
Yes	138 (79·8%)	573 (68·8%)	..
No	35 (20·2%)	260 (31·2%)	..

p values calculated using Mann-Whitney U tests, Pearson's Chi squared tests, and Fisher's exact tests when applicable. RSV=respiratory syncytial virus. *1 denotes most deprived, 5 denotes least deprived. †Severe disease includes adults indicated as requiring during admission: oxygen supplementation, high-flow nasal oxygen, non-invasive ventilation or continuous positive airway pressure, invasive ventilation or mechanical ventilation, and intensive care unit admission, and adults who died within 30 days of admission to hospital.

Table 1: **Demographic characteristics and comorbidities**

	Vaccinated (n=324)	Unvaccinated (n=682)	p value
Age, years	77·7 (1·3)	77·7 (1·4)	0·13
Sex	..	..	0·027
Female	153 (47·2%)	373 (54·7%)	..
Male	171 (52·7%)	309 (45·3%)	..
Ethnicity	..	..	0·88
White	292 (90·1%)	603 (88·4%)	..
Asian or Asian British	12 (3·7%)	30 (4·4%)	..
Black, Black British, Caribbean, or African	2 (0·6%)	9 (1·3%)	..
Mixed or multiple ethinic groups	1 (0·3%)	2 (0·3%)	..
Other	4 (1·2%)	10 (1·5%)	..
Missing	13 (4·0%)	28 (4·1%)	..
Index of Multiple Deprivation quintile*	..	..	0·11
1	76 (23·5%)	184 (27·0%)	..
2	49 (15·1%)	114 (16·7%)	..
3	46 (14·2%)	121 (17·7%)	..
4	69 (21·3%)	124 (18·2%)	..
5	83 (25·6%)	135 (19·8%)	..
Missing	1 (0·3%)	4 (0·6%)	..
Comorbidities			
At least one comorbidity	302 (93·2%)	625 (91·6%)	0·39
Chronic respiratory disease	204 (63·0%)	397 (58·2%)	0·15
Chronic neurological disease	80 (24·7%)	195 (28·6%)	0·19
Chronic liver disease	8 (2·5%)	21 (3·1%)	0·59
Chronic kidney disease	84 (25·9%)	175 (25·7%)	0·93
Chronic heart disease and vascular disease	202 (62·3%)	414 (60·7%)	0·62
Immunosuppression	97 (29·9%)	174 (25·5%)	0·14
Diabetes and other endocrine disorders	95 (29·3%)	198 (29·0%)	0·92
Morbid obesity	15 (4·6%)	33 (4·8%)	0·38
Severe mental illness	8 (2·5%)	25 (3·7%)	0·32

p values calculated using Mann-Whitney U tests, Pearson's Chi squared tests, and Fisher's exact tests when applicable. *1 denotes most deprived, 5 denotes least deprived.

Table 2: **Demographic characteristics and comorbidities by vaccination status**

Discussion

Using data from an active, national, hospital-based enhanced surveillance network in England (ie, HARISS), RSV pre-F vaccine (Abrysvo) showed 82% effectiveness against hospital admission for RSV-associated acute respiratory infection in adults aged 75–79 years in the first season since the introduction of the immunisation programme in the UK. Vaccine effectiveness was 77–89% across different presentations of RSV-associated infection, including exacerbations of chronic disease, and was maintained across different comorbidity groups including those with immunosuppression.

To our knowledge, our findings are among the first to show RSV vaccine effectiveness against hospital admission in older adults in Europe, with the potential to affect policy in the UK and other regions worldwide with similar health-care structures. Additionally, these

	Controls		Cases		Unadjusted vaccine effectiveness (95% CI)	Adjusted* vaccine effectiveness (95% CI)
	Unvaccinated	Vaccinated	Unvaccinated	Vaccinated		
Severe disease†	362	211	128	10	86·6 (75·2–93·5)	86·7 (75·4–93·6)
Reason for hospital admission						
Admitted with LRTI	361	200	97	6	88·8 (76·1–95·7)	88·6 (75·6–95·6)
Lung disease exacerbation‡	129	81	36	5	77·9 (46·0–92·6)	77·4 (42·4–92·8)
Lung disease, heart disease, or frailty exacerbation‡	142	88	40	5	79·8 (51·3–93·2)	78·8 (47·8–93·0)
Comorbidity group						
Immunocompetent	391	218	117	9	86·2 (73·7–93·6)	86·2 (73·6–93·6)
Immunosuppression	134	90	40	7	73·9 (42·6–89·7)	72·8 (39·5–89·3)
Chronic heart and vascular disease	317	189	97	13	77·5 (60·2–88·3)	77·0 (59·1–88·0)
Chronic respiratory disease	314	194	83	10	80·5 (63·2–90·7)	80·1 (62·4–90·6)
Overall	**525**	**308**	**157**	**16**	**82·6 (71·3–90·2)**	**82·3 (70·6–90·0)**

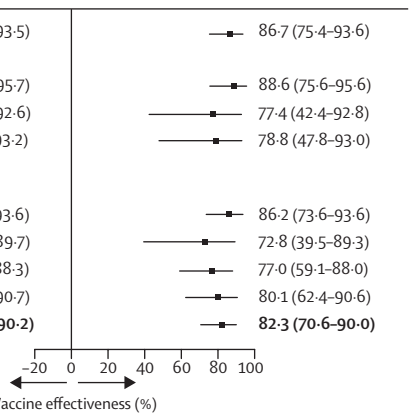

Figure 3: **Estimated vaccine effectiveness against hospital admission for respiratory syncytial virus-associated acute respiratory infection in 2024–25**
LRTI=lower respiratory tract infection. *Vaccine effectiveness adjusted for days from start of the surveillance period to hospital presentation using splines and presence of at least one comorbidity or immunosuppression, or both. †Severe disease includes requirement of oxygen supplementation, high-flow nasal oxygen, non-invasive ventilation or continuous positive airway pressure, invasive ventilation or mechanical ventilation, and admission to the intensive care unit on hospital admission and adults who died within 30 days of hospital admission. ‡No LRTI.

findings provide new evidence on RSV vaccine effectiveness in adults admitted due to RSV-associated chronic illness exacerbations, such as exacerbations of COPD. These additional data are important to direct vaccine policy and support cost-effectiveness evaluations, particularly for programmes that might be focused on individuals living with major comorbid conditions.

The RENOIR clinical trial for the RSV pre-F vaccine reported vaccine efficacy of 85·7% (96·66% CI 32·0–98·7) against RSV with at least three lower respiratory symptoms or signs during the first season.[9] Although there are differences in the endpoint studied and population characteristics, such as the age range of older adults included, our findings are consistent with the trial data, with both studies demonstrating substantial vaccine protection.

Furthermore, real-world studies of RSV vaccine effectiveness conducted in the USA have reported effectiveness against hospital admission in older adults of 80·3% (95% CI 65·8–90·1),[13] 75·5% (73·1–77·6),[16] 75% (50–87),[15] and 89% (52–97)[12] when emergency department visits were also included, and 80% (71–85) in older adults who were immunocompetent and 73% (48–85) in those who were immunosuppressed.[14] Vaccine effectiveness, specifically for the RSV pre-F vaccine, has been reported between 73% and 89%.[12–14] Our overall estimate of vaccine effectiveness is consistent with these previous studies, with overlapping 95% CIs. Although our study focuses on individuals aged 75–79 years only (compared with previous studies focusing on adults aged 60 years and above) vaccine effectiveness across different age groups (60–74 years and ≥75 years) has been reported to be similar.[14–16]

When focusing on more severe disease including hospital admissions requiring oxygen supplementation, the point estimate for vaccine effectiveness was higher at 86·7%, although the 95% CIs overlapped with the overall vaccine effectiveness estimates. In another study assessing RSV vaccine effectiveness among adults with severe disease, vaccine effectiveness was 91% in severe RSV-related lower respiratory tract disease compared with 89% in the whole cohort,[12] although with wide and overlapping 95% CIs. By contrast with our study, oxygen use was the only disease severity outcome used. For other respiratory virus vaccines, such as the COVID-19 vaccine, higher vaccine effectiveness against more severe disease has been observed.[27]

Exacerbations of chronic disease, especially chronic heart or lung disease, account for a large proportion of hospital admissions due to RSV infection.[4,5] Tseng and colleagues reported that 80·4% of older adults with COPD, chronic bronchitis, or emphysema had an exacerbation of these chronic lung diseases during hospital admission for RSV infection,[28] emphasising a key opportunity for prevention of severe illness through vaccination. Our study provides evidence of vaccine effectiveness in adults admitted due to lower respiratory tract infection (88·6%) and exacerbations of chronic illness (77·4%); point estimates were higher in those presenting with lower respiratory tract infection, although 95% CIs overlapped. It will be important for future studies to determine whether this potential difference in vaccine effectiveness is statistically significant. The clinical impacts and outcomes of RSV-associated lower respiratory tract infection (including pneumonia) differ compared with exacerbations of

chronic illnesses, and differences in vaccine effectiveness according to these different presentations would influence future modelling and cost-effectiveness assessments.

Older adults with immunosuppression comprised a large proportion of the study cohort (26·9%), underlining the risks posed to these individuals from RSV infection. Individuals with immunosuppression were excluded from the RENOIR trial[9] and, therefore, this study adds important insights to the evidence base. We observed a vaccine effectiveness against hospital admission of 72·8% among individuals with immunosuppression; this point estimate was lower than for individuals who were immunocompetent, but the 95% CIs overlapped. This finding is consistent with a study conducted in the USA in adults who showed similar vaccine effectiveness in those who were immunocompromised (73% *vs* 80% in those who were immunocompetent),[14] with overlapping confidence intervals.

The substantial vaccine protection reported in our study across different reasons for hospital admission and comorbidity groups, including immunosuppression, underscores the importance of RSV vaccination in reducing severe outcomes faced by at-risk populations, including older adults and those with chronic medical conditions.[29,30] Strategies that promote high vaccine coverage are important—particularly in populations with lower coverage.[8] Our analyses indicate that vaccination of other age groups and/or clinical risk groups might be considered by National Immunisation Technical Advisory Groups alongside other data on burden, cost-effectiveness, and vaccine effectiveness in other age groups.

Strengths of this study include the use of a national, sentinel surveillance system for acute respiratory infection with strong geographical representation across England, increasing its generalisability. The distribution of ethnicities in the study reflects national trends in census data for adults aged 65 years and older,[23] supporting representativeness. HARISS is an active, enhanced surveillance system collecting data to meet this study's aims. This surveillance system enables the collection of data on specific reasons for admission and outcomes among those who meet a case definition and, therefore, does not rely on routine data sources. The use of the HARISS network, where hospitals are recruited due to consistent routine molecular testing for RSV, influenza, and SARS-CoV-2 in older adults presenting with acute respiratory infection, reduces bias caused by selective testing. The direct review of patient notes by trained staff resulted in detailed clinical information being obtained. Furthermore, the inclusion of only admissions with respiratory virus swabbing within 48 h of presentation to hospital resulted in the inclusion of cases who had been admitted due to RSV-associated acute respiratory infection rather than nosocomial infection. The use of a national vaccination registry provided reliable reports of vaccination status.

There are several limitations of this study. The size of the study cohort did not allow assessment of vaccine effectiveness against more severe outcomes alone (ie, without oxygen supplementation) such as intensive care admission and death at 30 days. As the controls selected for this study were negative for RSV, influenza, and SARS-CoV-2, we were unable to conduct a sensitivity analysis using controls negative for RSV but positive for influenza and/or SARS-CoV-2. Testing was conducted as part of routine clinical care and not for research purposes. Therefore, there might be some variation in testing procedures between sites. Not all respiratory samples were tested using an extended respiratory viruses panel (eg, for rhinovirus). Therefore, we are unable to report this positivity information for the control group. Although we assessed relevant confounders and adjusted for them when appropriate in the analysis, residual confounding (eg, severity of chronic illness or other comorbidities such as musculoskeletal conditions) that is not captured in comorbidity data is possible. This study reports data from one RSV season, and duration of protection should be monitored over subsequent seasons. Lastly, we do not report subtyping data as this information was not available for all samples. Assuming the distribution of subtypes across the hospital population is similar to the wider community, both RSV-A and RSV-B subtypes were identified in similar proportions in all-age data from primary care practices over winter 2024–25 in England.[31] Further monitoring of vaccine effectiveness and genomic surveillance is warranted over different RSV seasons.

This study is among the first to present evidence of real-world effectiveness of the RSV pre-F vaccine against RSV-associated hospital admissions in older adults in Europe, including in those admitted due to exacerbations of chronic illness. The high vaccine effectiveness observed across different RSV-related presentations and in individuals with a range of underlying comorbid illnesses supports the promotion of high vaccine coverage to reduce RSV-associated illness in adults.

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Contributors

WSL, JLB, MZ, CW, RS, and HW conceptualised the study. WSL, JLB, CW, RS, and HW contributed to the methodology. RS, HW, and AC performed formal analysis and visualisation. RS and CR handled data curation. RS and HW had full access to and verified the data (not all co-authors were authorised access to all data for information governance reasons). RS, SA, DA, SB, CE, RG, JH, KH, OMK, AM, MOZ, EP, NR, GW, MZ, JLB, and WSL conducted the investigation. RS, SA, DA, SB, CE, RG, JH, KH, OMK, AM, MOZ, EP, NR, GW, MZ, JLB, and WSL managed resources. RS, SA, DA, SB, CE, RG, JH, KH, OMK, AM, MOZ, EP, NR, GW, MZ, JLB, and WSL carried out project administration. CR and RS developed the software. WSL, TM, CW, JLB, MZ, and HW supervised the project. RS, WSL, and JLB drafted the original manuscript. All authors participated in reviewing and editing the manuscript. All authors had final responsibility for the decision to submit for publication.

Declaration of interests

DA reports grants from the NIHR Advanced Fellowship in Pleural Infection and the University of Bristol. RG reports speaker fees and/or conference attendance (unrelated to paper topic matter) from AstraZeneca UK, Sanofi UK, and GSK UK; support for attending meetings or travel from Sanofi UK; and an unpaid presidential role for the British Society for Allergy and Clinical Immunology. MZ reports being a Chair of International Society for Influenza and other Respiratory Virus Diseases and membership of the New and Emerging Respiratory Virus Threats Advisory Group (NERVTAG), the Scientific Advisory Group for Emergencies (SAGE), and Joint Committee on Vaccination and Immunisation expert or working groups. CHW reports being an invited speaker at independently organised scientific and medical conferences, which are sponsored by vaccine makers. WSL reports institutional funding from UK Health Security Agency (WSL's institution is a lead coordinating institution of HARISS); unrestricted investigator-initiated institutional research funding from Pfizer, for an unrelated multicentre study in pneumonia in which WSL is the chief investigator (study ended Dec 31, 2023); being an unpaid Deputy Chair of Joint Committee on Vaccination and Immunisation; and an unpaid leadership role in the NIHR Respiratory Translational Collaboration, Acute Respiratory Infection National Research Strategy Group. TC reports grants or contracts from NIHR, Biomerieux/Biofire, Inflammatix, and SenseBio; consulting fees from Biomerieux/Biofire, Cepheid, Janssen, Sanofi, Synairgen, Harvey Medical, and IP Pragmatics; payment or honoraria from Cepheid, Qiagen, Biomerieux/Biofire, Janssen, and Medscape; support for attending meetings or travel from Cepheid, Roche diagnostics, Roche, Qiagen, and Janssen; participation on a data safety monitoring or advisory board for Roche, Shionogi, Roche Diagnostics, GSK, Seqirus, Sanofi, Cepheid, and Janssen; stock or stock options with Synairgen; and receipt of equipment, materials, drugs, medical writing, gifts, or other services from Biomerieux/Biofire, Qiagen, Lex diagnostics, and Abbott. MD reports subsidised attendance at a UK Clinical Virology Network scientific conference, which is a charity with partial financial support from companies active in respiratory virus diagnostics. No direct payments were received. The UKHSA Immunisation and Vaccine-Preventable Diseases Division undertakes post-marketing surveillance and analysis for vaccine makers, including Pfizer for RSV, for which it makes cost-recovery charges.

Data sharing

Original data are confidential, and no additional data are available.

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