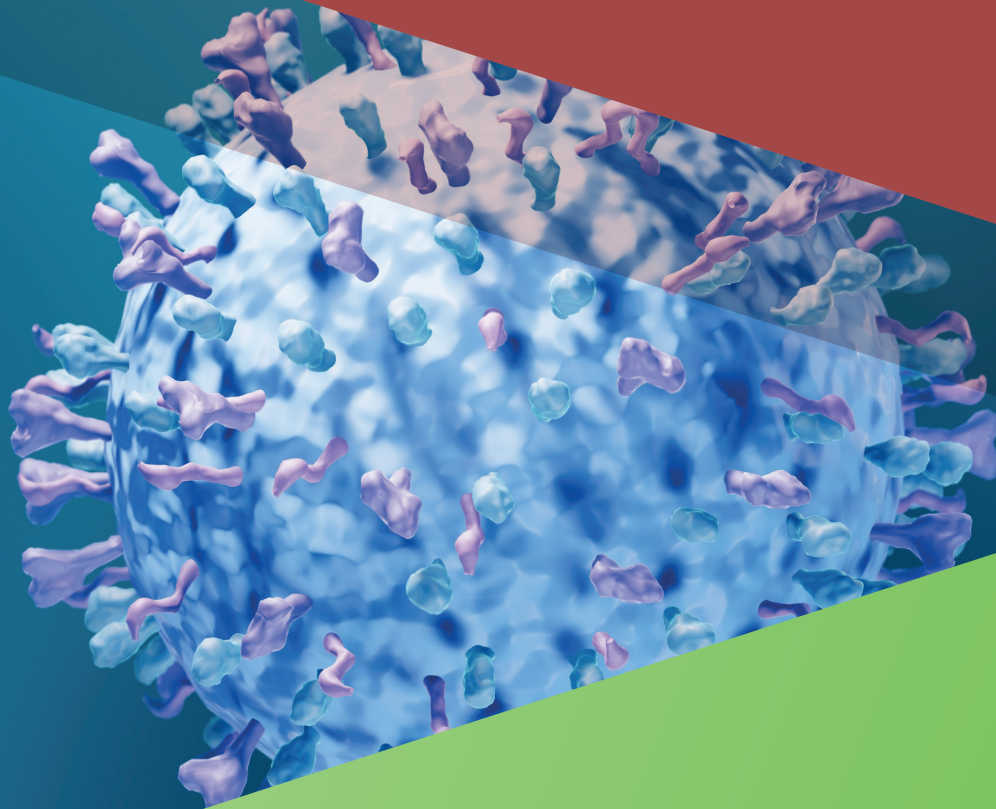


ASSESSMENT



**Rapid systematic review of
clinical risk factors for severe
Respiratory Syncytial Virus
infection in adults resulting in
hospitalisation, intensive care
unit admission or death**

ECDC ASSESSMENT

Rapid systematic review of clinical risk factors for severe Respiratory Syncytial Virus infection in adults resulting in hospitalisation, intensive care unit admission or death



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Declaration of interests

No conflicts of interest were reported by any members of the review team.

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Abbreviations

aHR	Adjusted hazard ratio
aOR	Adjusted odds ratio
ARI	Acute respiratory infection
CAD	Coronary artery disease
CHF	Chronic heart failure
CI	Confidence interval
CKD	Chronic kidney disease
CLD	Chronic liver disease
COPD	Chronic obstructive pulmonary disease
EU/EEA	European Union/European Economic Area
HR	Hazard ratio
ICU	Intensive care unit
OR	Odds ratio
PCR	Polymerase Chain Reaction
RoB	Risk of bias
RR	Risk ratio
RSV	Respiratory syncytial virus

Executive summary

Respiratory syncytial virus (RSV) can cause severe respiratory illness in older adults and those with underlying comorbidities. With the recent approval of vaccines against RSV and other preventive interventions, there is a need to clarify which clinical risk factors are most strongly associated with severe outcomes in adults. This rapid systematic review aimed to identify and assess the strength and consistency of associations between clinical risk factors and severe RSV outcomes in adults, to inform risk stratification and support evidence-based prioritisation of vaccination and other preventive interventions in high-risk populations in the European Union/European Economic Area (EU/EEA).

Methods

This review included peer-reviewed articles comprising study cohorts of adults (≥ 18 years) with laboratory-confirmed RSV infection that reported associations between predefined clinical risk factors and severe outcomes. Records were identified through searches in electronic databases (Embase, Cochrane Library and PubMed, including MEDLINE) and by screening reference lists of included articles. Effect estimates were interpreted using predefined thresholds. Relative effects of 1.1 to <1.5 were categorised as weak, 1.5 to <2.0 as moderate, 2.0 to <4.0 as strong, and ≥ 4.0 as very strong. These thresholds were applied as a descriptive framework to support interpretation across heterogeneous studies and should not be taken to imply comparability of baseline risk, outcome prevalence, or clinical context. Priority was given to findings from low risk of bias studies and adjusted estimates.

The database search identified 1 594 records. After the removal of duplicates, 1 134 records remained. Title and abstract screening excluded 994 records, leaving 140 articles for full-text review. Of these, eight articles met the inclusion criteria. One additional relevant article was identified through reference list screening, resulting in a total of nine included articles.

Key findings

The evidence base was dominated by retrospective hospital-based cohort studies, focused on older (>60 years) adult populations. Studies were heterogeneous in terms of study design, population characteristics, definitions of exposures and outcomes, and analytical methods, limiting comparability and precluding definitive ranking of risk factors or quantitative synthesis by meta-analysis. With the exception of age, most studies assessed risk factors as binary variables, limiting the ability to examine gradients of risk or associations across levels of the risk factor (e.g. varying degrees of disease or differences in biomarker levels).

Demographic factors

Older age, particularly 65–75 years and above, was among the most frequently evaluated risk factors for severe RSV outcomes across the included studies. Some evidence, particularly from a low risk-of-bias study in older populations, suggests an increased risk with advancing age, especially for mortality, with higher risks observed in the oldest age groups. However, findings were not consistent across all studies, including those at low risk of bias, and several analyses showed no statistically significant association. Where associations were observed, they were often imprecise and not always robust to adjustment for confounding. The overall evidence base is limited, and the observed associations may in part reflect residual confounding by frailty and underlying health status. Taken together, older age is likely to be an important risk factor for severe RSV outcomes, particularly mortality, but uncertainty remains regarding the strength and consistency of this association. While not all studies showed consistent effects, and some estimates were imprecise, the overall evidence suggests that advancing age is the most important and policy-relevant risk factor. Sex was not supported as an independent risk factor in the more robust analyses.

Comorbidity factors

Among comorbidities, chronic lung disease, particularly chronic obstructive pulmonary disease (COPD), showed some evidence of increased risk. Moderate to strong associations were reported across several studies, especially for hospitalisation, although these were largely based on unadjusted analyses, some effects were attenuated after adjustment, and evidence for more severe outcomes was inconsistent and limited.

Neurological disease was associated with an increased risk in a limited number of studies, including low risk of bias studies reporting moderate adjusted effects. This suggests a plausible association, although the evidence base remains small.

Cancer and haematological malignancies were associated with increased mortality in a small number of studies, with some strong to very strong adjusted estimates reported. However, these findings are based on limited data.

Cardiovascular and cerebrovascular diseases showed inconsistent associations. While some studies reported moderate to strong effects, findings were not consistent across studies or outcomes, and the independent contribution of these conditions remains uncertain.

For diabetes, kidney disease, and liver disease, the evidence was limited or inconsistent, with no clear or consistent associations identified.

Immunosuppression

Evidence for immunosuppression as a risk factor was limited and inconsistent. Most studies did not find a clear association, and definitions varied. Overall, current evidence is insufficient to determine whether immunosuppression independently increases the risk of severe RSV outcomes in adults.

Lifestyle factors

Smoking showed some suggestive evidence of increased risk, with moderate adjusted and strong crude associations reported in individual studies. However, findings were not consistent across outcomes, and evidence remains limited and largely based on analyses that did not consistently account for key confounders such as age and comorbid conditions, limiting interpretation of independence of effect. Obesity was assessed in only one study, with no clear association observed.

Conclusion

In conclusion, despite small and underpowered cohorts and the inability to perform a meta-analysis, the evidence most consistently identifies older age as an important risk factor, with the strongest and most consistent evidence among comorbidities observed for chronic lung diseases, particularly COPD. Evidence for other comorbidities is less consistent: neurological disease and cancer or haematological malignancies show suggestive associations, whereas cardiovascular disease and other conditions are supported by limited or inconsistent findings. Most available studies assess effects in older adult cohorts. These findings can inform prioritisation of high-risk groups for RSV vaccination.

Evidence gaps and future research priorities

Evidence on clinical risk factors for adults under 60 years, immunosuppressed people, and those with multimorbidity is very limited. Most studies focus on RSV disease progression among hospitalised patients, with few comparing community-managed versus hospitalised patients or reporting outcomes by type or degree of immunosuppression. Interaction effects between risk factors and the potential compounded impact of multimorbidity are also poorly characterised, leaving potential uncertainty about which groups are at highest risk. Future research should prioritise large, sufficiently powered, prospective cohort and case-control studies. Greater inclusion of younger adults (<60 years), immunocompromised individuals, and people with diverse comorbidity profiles would strengthen risk stratification and better inform targeting of preventive strategies for severe RSV disease. Furthermore, inclusion of longer-term outcomes (e.g. 1–5-year morbidity and mortality) would support better characterisation of both the immediate and sustained impact of RSV infection.

1. Introduction

1.1 Rationale

Respiratory syncytial virus (RSV) is increasingly recognised as a significant cause of severe respiratory illness in older adults and those with underlying medical conditions. Although historically associated with paediatric disease, RSV infection is now known to contribute substantially to morbidity, hospitalisation, intensive care unit (ICU) admission and mortality among adults, particularly in ageing populations. In the EU, an estimated 160,000 RSV-associated hospitalisations occur annually among adults (≥ 18 years), with 92% of these hospitalisations occurring in adults aged 65 years and above [1]. For comparison, an estimated 250,000 RSV-associated hospitalisations occur annually among young children (0-4 years) [1,2].

In the EU/EEA, several interventions have been authorised to protect against lower respiratory tract disease caused by RSV across different age groups. Interventions licenced specifically for adults are summarised in Table 1.

Table 1. RSV vaccines authorised by European Medicines Agency for adults [3-5]

Brand name	Manufacturer	Vaccine type	Authorisation	Approved age group / population
Arexvy	GSK	Protein subunit + adjuvant	June 2023	Adults ≥ 18 years
Abrysvo	Pfizer	Protein subunit	August 2023	Adults ≥ 18 years; pregnant women to protect their infants
mResvia	Moderna	mRNA vaccine	August 2024	Adults ≥ 18 years

This rapid systematic synthesis of available evidence on clinical risk factors for severe RSV outcomes – including hospitalisation, ICU admission, and death – aims to support:

- **Improved understanding of at-risk populations:** Identifying which clinical risk factors are most strongly associated with severe RSV outcomes will improve understanding of risk stratification for severe disease in adults.
- **Evidence-based recommendations for targeting interventions:** EU/EEA countries are currently implementing or planning RSV vaccination and other preventive strategies. This review will provide a scientific basis to inform **prioritisation of adult subpopulations** for RSV vaccination and other public health interventions.
- Given the recent licensure of RSV vaccines for adults in the EU/EEA, timely evidence is critical to ensure that **prevention efforts are targeted effectively to reduce disease burden**, particularly among identified high-risk groups.

1.2 Objectives

The aim of this rapid review was to determine the clinical risk factors associated with hospitalisation, ICU admission, and death, in adults following infection with RSV, based on the available literature.

2. Methods

2.1 Criteria for considering studies for the rapid systematic review

2.1.1 Eligibility criteria

This rapid review was conducted in accordance with Cochrane methods guidance for rapid systematic reviews, applying the following restrictions to scope [6]:

- Focusing on clinical risk factors as measurable characteristics or conditions present in patients and include both demographic and health-related variables that are clinically relevant and biologically plausible in affecting disease progression or outcome.
- Including only publications that compared outcomes within groups diagnosed with RSV and excluding those that compared people with RSV to those without RSV infection.
- Focusing only on published articles and articles-in-press to ensure that only results that had been peer-reviewed were included in the final analysis.

Elements of the research question are presented in the Population, Exposure, Comparator, Outcomes, and Study design (PECOS) framework in Table 2.

Table 2. Population, Exposure, Comparator, Outcomes, and Study design (PECOS) framework, study inclusion and exclusion criteria

Category	Inclusion criteria	Exclusion criteria
Population	Human adults (≥ 18 years) with confirmed RSV infection, verified by nucleic acid amplification test (NAAT) – such as real-time reverse transcription polymerase chain reaction (RT-PCR) – or by rapid antigen testing. Studies stating a requirement for laboratory-confirmed RSV infection, that did not specify the laboratory test used, were included.	Studies focusing on RSV infection in children or mixed-age populations without separate data for adults were excluded.
Exposure	The exposures considered are clinical risk factors, i.e. demographic factors (e.g. age, sex), comorbidity factors, immunosuppression, and lifestyle factors (e.g. smoking status). For all studies, data were also extracted on RSV type (A or B), as well as on delays to diagnosis or treatment, if reported, to help identify whether these factors also contributed to disease severity in addition to the clinical risk factors. Where possible, RSV type and supportive treatment were held constant to allow for comparability across studies.	Studies investigating clinical risk factors for acquiring RSV infection, rather than clinical risk factors for severe disease outcomes (hospitalisation, ICU admission, or death), were excluded. Studies exclusively assessing clinical signs, investigations or treatments at time of presentation. Studies examining non-clinical risk factors (e.g. environmental or socioeconomic) without clinical relevance were excluded.
Comparator	Individuals without the specified clinical risk factor.	
Outcome	Clinical outcomes reflecting disease severity: no hospitalisation, hospitalisation, ICU admission, and death. The outcomes were used to evaluate how clinical risk factors influence progression of RSV infection in adults.	
Study design	Prospective and retrospective cohort studies, case-control studies, cross-sectional studies.	Simple prevalence studies or descriptive studies that did not quantify the association between candidate risk factors and disease severity using effect estimates (RR, OR or HR), but instead relied only on comparisons of group means, were excluded.
Timing	The rapid review included records published until 2 September 2025.	

Category	Inclusion criteria	Exclusion criteria
Geography	The geographic scope was focused by the search strategy to target studies reporting from Europe and a selection of other settings, such as Australia, Canada, New Zealand, Japan, South Korea, and the United States.	
Publication type	Peer-reviewed publications	Preprints, conference abstracts, and grey literature were excluded; only peer-reviewed, published studies were considered.
Language	As the search terms were in English, the search was limited to titles and abstracts in English. Articles written in other languages but with an English language abstract were also considered, according to the criteria listed below.	

2.1.2 Information sources

The following electronic databases were searched to identify published studies: Embase, PubMed (including MEDLINE), and the Cochrane Library.

2.1.3 Search strategy

The search strategy applied a mixture of general and database specific keywords in the title, abstract, or text of the source. The search strategy was subjected to internal critical scientific evaluation using the PRESS elements [7]. The report covers peer-reviewed articles published until 2 September 2025. There were no language restrictions, however search terms were in English. Details of the search are described in Annex 1. In addition, the reference lists of the included articles were searched to identify any further relevant publications.

2.1.4 Management of study records and quality control

References were managed using EndNote bibliographic software (Clarivate Analytics, Philadelphia, United States). Screening of title, abstract, and full text was conducted by independent reviewers (DS, JK, SH, AA, PJ and CN) using the Population, Exposure, Comparison, Outcome, Study design (PECOS) approach. Inter-rater agreement was ensured for all steps, and any disagreements were discussed to adjust the approach and maintain consistency. Calibration tests were completed to ensure a minimum inter-rater agreement of 90% in the screening process for the full text screening. The calibration test was performed on 10 randomly selected records at title and abstract screening, conducted by five reviewers, where the kappa (κ) value was 0.63 (CADIMA classification: 'good'), and on seven randomly selected records at full-text screening, conducted by three reviewers, where inter-rater agreement was 100% ($\kappa = 1.0$). A 10% sample of records was additionally checked by a member of the lead team, and constructive feedback and re-training were undertaken if reviewer agreement fell below 90%. In addition, 10 likely-to-be-included articles were sent to the review coordination team at ECDC for checking. The online platform CADIMA (Julius Kühn-Institut, Quedlinburg, Germany) was used for managing and screening of records [8].

2.1.5 Data extraction

Data for the following variables were extracted using a pre-defined data extraction form:

- Publication year
- First author
- Title
- Country
- Data source
- Study design
- Study objective
- Study duration
- Population overview
- Diagnostic methods for RSV
- Diagnosis/treatment delays
- Total number of participants
- Outcome comparisons
- Sample frame number of participants
- Statistical methods
- Authors' conclusions
- Comments

Furthermore, for each relevant clinical risk factor reported, the following information was extracted:

- Crude effect estimates
- Adjusted effect estimates

Effect estimates were interpreted using predefined thresholds. Relative effects of 1.1 to <1.5 were categorised as weak, 1.5 to <2.0 as moderate, 2.0 to <4.0 as strong, and ≥ 4.0 as very strong. These thresholds were applied to facilitate structured comparison and synthesis of associations across studies with heterogeneous designs and populations. This categorisation was intended as a descriptive framework to support consistency in interpretation and does not account for baseline risk, outcome prevalence, or clinical context. Where available, confidence intervals and study-level risk of bias were considered alongside effect magnitude during interpretation.

2.1.6 Quality appraisal

Risk of bias (RoB) was assessed using the JBI Critical Appraisal Checklists for Cohort Studies [9] and each article was given a global RoB score; low, medium or high.

2.1.7 Meta-analysis

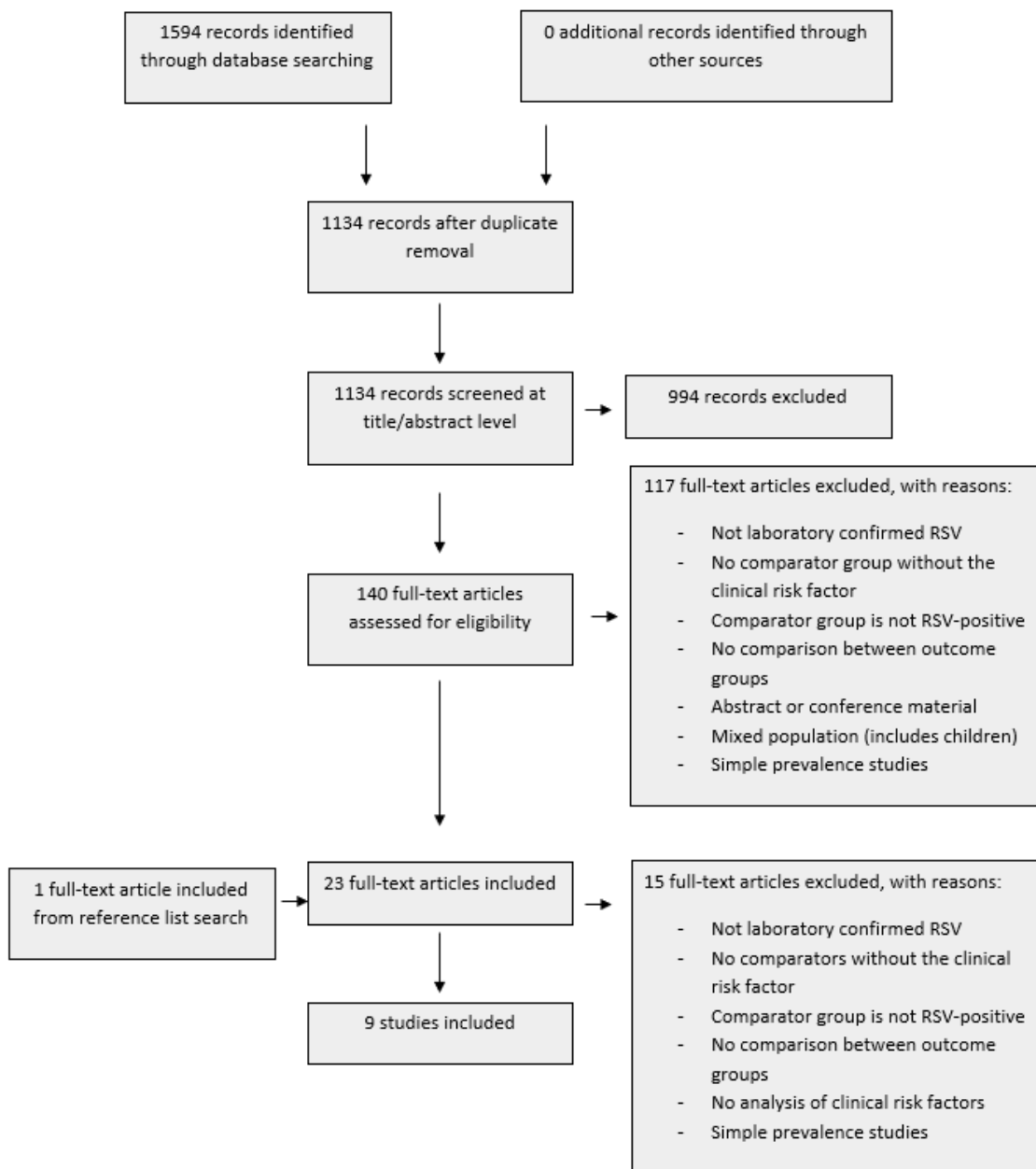
Following data extraction and quality appraisal, a feasibility assessment was conducted to determine whether the results from the included studies could be pooled to estimate the association between each risk factor and the selected outcomes. Specifically, study populations, definitions of exposures (risk factors), and effect measures were reviewed to assess their comparability and alignment across studies. The planned approach was to extract effect estimates (odds ratios, risk ratios, or hazard ratios) with corresponding 95% confidence intervals and combine these using random-effects models to account for between-study variability. Heterogeneity was to be assessed through visual inspection of forest plots and quantified using the I^2 statistic. In the absence of sufficient comparability in outcome definitions, effect measures, or reported data, a narrative synthesis was conducted.

3. Results

3.1 Literature search

Database searches yielded a total of 1 594 hits. After the removal of duplicates, a total of 1 134 articles were eligible for title and abstract screening. Of these, 140 articles were found eligible for full text screening and, based on those, 23 articles proceeded to data extraction. During the data extraction process, 15 articles were excluded upon closer examination, as they did not fully meet the pre-defined inclusion or exclusion criteria. Eight articles proceeded for data synthesis. Cross-searching the reference lists of the included studies identified one additional article that was eligible for inclusion. In total, nine articles were included (Figure 1).

Figure 1. Flow-chart of the screening and inclusion of records for this rapid review



All of the included articles were cohort studies with seven retrospective [10-16] and two prospective studies [17,18]. Publication year ranged from 2013 to 2025, and study periods ranging from 2005 to 2024. Five of the articles were from Europe (Austria, Cyprus, Italy, Spain and Switzerland) [11,13-16], while four were from the United States [10,12,17,18]. A summary of included articles can be seen in Table 3.

Table 3. Summary of included articles

Author, year	Country	Study design	Study population		Outcome comparison				Risk factors assessed	Statistically significant individual risk factors ^a
			Eligible	Included [mean/median age]	Severe	n	Less severe	n		
Ma, 2025 [17]	US (20 States)	Prospective multicentre (26 hospitals) cohort study	1 111 adults ≥18 years old with laboratory-confirmed RSV	397 adults aged 18-59 years Hospitalisation: median age 49 years [IQR 38-55] ICU: median age 48 years [IQR 38- 55]	ICU	96	Hospitalisation	301	Comorbidity factors: • LD: COPD	Comorbidity factors: • LD: COPD
				714 adults ≥ 60 years Hospitalisation: median age 73 years [IQR 66- 81] ICU: median age 71 years [IQR 67- 77]	ICU	164	Hospitalisation	550		
Joseph, 2025 [11]	Switzerland	Retrospective single-centre hospital cohort study	153 adults ≥18 years old who were hospitalised for at least one night with a laboratory-confirmed RSV infection	136 Median age: 79 years [IQR 66- 81]	ICU, death	25	Hospitalisation	111	Comorbidity factors: • LD: asthma, COPD • CV: CAD or MI, peripheral arterial disease, stroke or transient ischaemic attack, arrhythmia • DB: diabetes • KD: CKD • LiD: chronic liver disease • Ca: chronic haematological disease Immunosuppression*	Comorbidity factors: • KD: CKD

Author, year	Country	Study design	Study population		Outcome comparison				Risk factors assessed	Statistically significant individual risk factors ^a
			Eligible	Included [mean/median age]	Severe	n	Less severe	n		
					ICU	19	Hospitalisation	117	Comorbidity factors: <ul style="list-style-type: none"> • LD: asthma, COPD • CV: CAD or MI, peripheral arterial disease, stroke or transient ischaemic attack, arrhythmia • DB: diabetes • KD: CKD • LiD: chronic liver disease • Ca: chronic haematological disease Immunosuppression	<ul style="list-style-type: none"> • Immunosuppression
					Death	9	Hospitalisation	127	Comorbidity factors: <ul style="list-style-type: none"> • LD: asthma, COPD • CV: CAD or MI, peripheral arterial disease, stroke or transient ischaemic attack, arrhythmia • DB: diabetes • KD: CKD • LiD: chronic liver disease • Ca: chronic haematological disease Immunosuppression	Comorbidity factors: <ul style="list-style-type: none"> • KD: CKD

Author, year	Country	Study design	Study population		Outcome comparison				Risk factors assessed	Statistically significant individual risk factors ^a
			Eligible	Included [mean/median age]	Severe	n	Less severe	n		
Haeberer, 2024 [16]	Spain	Retrospective multicentre (two hospitals) cohort study	Centralised microbiology database (MICROB) database data on adult patients ≥60 years with confirmed RSV infection	706 Hospitalisation: mean age 79.5 years (SD 9,4) No mean age reported for the severe outcome group	Prolonged hospital stay, readmission, ICU or death	Composite number not reported. Among the hospitalised RSV population, 41 were admitted to ICU and 73 died during admission	Hospitalisation	635	Demographic factors: <ul style="list-style-type: none"> • Sex Comorbidity factors: <ul style="list-style-type: none"> • LD: chronic lung disease • CV: cardiovascular/cerebrovascular disease • KD: CKD • LiD: liver disease • ND: neurological condition • Other: endocrine or metabolic disorder Immunosuppression: <ul style="list-style-type: none"> • Immunocompromising condition (not specified) Lifestyle factors: <ul style="list-style-type: none"> • Smoker (current or previous) 	
					Hospitalisation	71	No hospitalisation	635	Demographic factors: <ul style="list-style-type: none"> • Sex Comorbidity factors: <ul style="list-style-type: none"> • LD: chronic lung disease • CV: cardiovascular/cerebrovascular disease • KD: CKD • LiD: liver disease • ND: neurological condition • Other: endocrine or metabolic disorder Immunosuppression:	Comorbidity factors: <ul style="list-style-type: none"> • LD: chronic lung disease • CV: cardiovascular/cerebrovascular disease • ND: neurological condition Lifestyle factors: <ul style="list-style-type: none"> • Smoker (previous) Note: the specific adjustment factors were not reported

Author, year	Country	Study design	Study population		Outcome comparison				Risk factors assessed	Statistically significant individual risk factors ^a
			Eligible	Included [mean/median age]	Severe	n	Less severe	n		
									<ul style="list-style-type: none"> Immunocompromising condition (not specified) Lifestyle factors: Smoker (current or previous)	
Boattini, 2023 [15]	Portugal, Italy, Cyprus	Retrospective multicentre (three hospitals) cohort study	Hospital records of adults ≥18 years hospitalised with community acquired pneumonia confirmed by PCR	74 Mean age: 71.2 years (SD 16,9)	Death during hospitalisation	10	Hospitalisation	64	Demographic factors: <ul style="list-style-type: none"> Age Sex Comorbidity factors: <ul style="list-style-type: none"> LD: asthma, COPD, sleep apnoea CV: CHF DB: diabetes KD: CKD 	No statistically significant individual risk factors were identified.
Goldman, 2022 [10]	US (New York)	Retrospective multicentre (three hospitals) surveillance study	Hospital records of adults ≥18 years, hospitalised ≥24h infected with lab-confirmed RSV and ≥2 acute respiratory illness symptoms	403 Median age: 69 years (IQR: 57-82)	ICU, mechanical ventilation, death during hospitalisation	77	Hospitalisation	326	Demographic factors: <ul style="list-style-type: none"> Age Sex Living in a care facility Comorbidity factors: <ul style="list-style-type: none"> LD: COPD, asthma, any respiratory conditions CV: any cardiac conditions, CHF ND: any neurological conditions Immunosuppression: <ul style="list-style-type: none"> Immunosuppressive conditions (not specified) Lifestyle factors: <ul style="list-style-type: none"> Obesity 	Comorbidity factors: <ul style="list-style-type: none"> COPD

Author, year	Country	Study design	Study population		Outcome comparison				Risk factors assessed	Statistically significant individual risk factors ^a
			Eligible	Included [mean/median age]	Severe	n	Less severe	n		
Schubert, 2021 [13]	Austria	Retrospective single centre hospital cohort study	Adult patients (age not specified) with lab-confirmed RSV	103 Median age: 57 years (IQR: 40-73)	Hospitalisation	45	No hospitalisation	58	Demographic factors: • Age (>65) Comorbidity factors: • LD: respiratory illness • CV: cardiac illness • DB: diabetes type II • KD: dialysis • Ca: oncological illness • Other: solid organ transplant Lifestyle factors: • Smoking	Hospitalisation vs. no hospitalisation Demographic factors: • Age (>65) Comorbidity factors: • LD: respiratory illness • CV: cardiac illness • DB: diabetes Lifestyle factors: • Smoking ICU admission vs. hospitalisation Comorbidity factors: • LD: respiratory illness
					ICU	7		45		
					Death	3		45		
Boattini, 2021 [14]	Portugal, Italy, Cyprus	Retrospective multicentre (3 hospitals) study	Hospitalised adults ≥65 years for community acquired RSV, confirmed within 72h by PCR	166 Mean age: 80.9 years (SD: 8,7)	Death during hospitalisation	20	Hospitalisation	146	Demographic factors: • Age • Sex Comorbidity factors: • Ca: solid neoplasm • Other: obstructive sleep apnoea/obesity hypoventilation system	Demographic factors: • Sex (male) Comorbidity factors: • Ca: solid neoplasm • Other: obstructive sleep apnoea/obesity hypoventilation system
Tseng, 2020 [12]	US (California)	Retrospective single centre hospital cohort study	Hospitalised adults ≥60 years with lab-confirmed RSV infection	664 Median age: 78 years (range: 60-103)	Death	75	Survival short term (≤60 days)	589	Demographic factors: • Age • Sex Comorbidity factors: • CV: CHF • KD: end stage renal disease • Ca: lymphoma	Death vs. survival short term (≤60 days) Demographic factors: • Age (85+ years vs. 60-64 years) Comorbidity factors: • Ca: lymphoma
					Death after hospitalisation	171	Survival long term (1-365 days)	493		

Author, year	Country	Study design	Study population		Outcome comparison				Risk factors assessed	Statistically significant individual risk factors ^a
			Eligible	Included [mean/median age]	Severe	n	Less severe	n		
									<ul style="list-style-type: none"> • ND: dementia 	Death vs. survival long term (1-365 days) Demographic factors: <ul style="list-style-type: none"> • Age (75-84 years vs. 60-64 years) • Age (85+ years vs. 60-64 years) Comorbidity factors: <ul style="list-style-type: none"> • CV: congestive heart failure • KD: end stage renal disease • Ca: lymphoma • ND: dementia
Walsh, 2013 [18]	US (New York)	Prospective single centre hospital cohort study	111 adults ≥21 years with RSV confirmed by PCR test	111 Hospitalisation: mean age 70.5 years (SD: 14,7) No hospitalisation: mean age 56,7 years (SD: 17,1)	Hospitalisation	50	No hospitalisation	61	Demographic factors: <ul style="list-style-type: none"> • Age • Sex Comorbidity factors: <ul style="list-style-type: none"> • Other: underlying conditions (including CHF, CAD, COPD, diabetes) 	Demographic factors: <ul style="list-style-type: none"> • Sex (female) Comorbidity factors: <ul style="list-style-type: none"> • Other: underlying conditions (including CHF, CAD, COPD, diabetes)

^a Statistical significance of individual risk factors: non-bold = statistically significant crude effect estimate; bold = statistically significant after adjustment of factors including at least age.

IQR (interquartile range), SD (standard deviation); Comorbidity factors: LD (lung disease), CV (cardiovascular and cerebrovascular disease), DB (diabetes), KD (kidney disease), LiD (liver disease), ND (neurological disease), Ca (cancer and haematological disease); COPD (chronic obstructive pulmonary disease); CAD (coronary artery disease); MI (myocardial infarction); CHF (congestive/chronic heart failure); CKD (chronic kidney disease).

* Specified as one or more of the following conditions: HIV/AIDS, history of organ transplantation, chemotherapy, prolonged corticosteroid use, or immunomodulating medications.

3.2 Quality appraisal

The articles included in this rapid review were all cohort studies; seven articles were retrospective and two were prospective. Overall, the included articles were assessed as being of satisfactory quality, with four articles having a low RoB [10,12,16,17], three articles having a medium RoB [13-15], and two having a high RoB [11,18], based on the global RoB score (see Table 4 for further details). Those rated as medium risk were mainly limited by incomplete control for confounding and unclear ascertainment of comorbidities or exposures, as well as some limitations in the reporting of follow-up and statistical analyses. The two studies assessed as high risk were primarily affected by insufficient information on recruitment strategies, incomplete reporting of exposure and outcome data, and inconsistencies between reported results and underlying data, limiting confidence in the validity of the findings.

Table 4. Quality assessment

First author, publication year	Global risk of bias score	Comments
Ma, 2025 [17]	Low	
Haeberer, 2024 [16]	Low	
Goldman, 2022 [10]	Low	
Tseng, 2020 [12]	Low	
Boattini, 2023 [15]	Medium	There is limited information on how exposures and confounding factors were defined and measured, and strategies to address confounding are not clearly described. Follow-up completeness is not reported, and no clear methods to address missing data are provided. In addition, although regression analyses were conducted, the statistical approach is insufficiently described, and subgroup sample sizes are small, limiting the robustness of the findings.
Boattini 2021 [14]	Medium	The study used multivariable regression analyses to adjust for confounding; however, exposure measurement is not clearly described, and the selection of variables based on univariable significance may have resulted in residual confounding. The relatively small sample size and limited number of outcome events further reduce the precision of the estimates.
Schubert, 2021 [13]	Medium	There is no mention of confounding or any adjustment for confounding. Only unadjusted estimates are presented. The sample size is small, and the number of outcome events is limited, especially deaths where the number is three. It is not entirely clear how patients were referred to the hospital where the study took place, or how the study population of 103 hospital admissions differed from the 45 patients who required in hospital care. There also appear to be errors in some reported data. For example, in Table 2 the odds ratios and confidence intervals do not match the reported p values for some clinical factors.
Joseph, 2025 [11]	High	Even though appropriate statistical models are used, including regression models with adjustment for confounding factors, there are errors in both the raw numbers and the reported percentages. The numbers listed in Tables 1 and 2 and in the text are not consistent, so the true values remain unclear. In addition, the numbers for the outcomes in Table 3 are small, with fewer than 10 events.
Walsh, 2013 [18]	High	The number of people enrolled in the first cohort is unknown, and the recruitment strategy is also unknown. There is no description of how demographic or medical history information was obtained, whether it was self-reported or taken from medical records or databases. The statistical methods used for the results in Table 1 are not described. There are also discrepancies between the raw data and the reported percentages.

3.3 Clinical risk factors for severe RSV disease

3.3.1 Demographic factors

Age

A total of six studies evaluated the association between older age and severe RSV disease in adults. Of these, two were assessed as having low RoB, three as medium, and one as high. Most studies were hospital-based cohorts or retrospective database analyses conducted in high-income countries between 2005 and 2008, 2011 and 2015 or 2017 and 2019. The outcome comparison was most commonly hospitalisation versus more severe outcome.

Table 5 summarises the findings of included studies assessing age as a risk factor for severe RSV outcomes, by RoB, comparison group, and publication year.

Description of evidence

Across studies, the mean or median age of participants ranged from 56 to 81 years, and the populations ranged from including people aged ≥ 18 years to only including people aged ≥ 65 years. Studies including younger adult populations (e.g. ≥ 18 years) did not consistently identify an association between age and severe outcomes, whereas studies restricted to older populations (≥ 60 or ≥ 65 years) more often reported an increased risk with advancing age. Most studies compared outcomes between predefined age categories (e.g. ≥ 65 vs < 65 years), although some modelled age as a continuous variable.

Several studies, including the low RoB study by Goldman et al. 2022 [10], did not show a significant age effect, but small sample sizes often resulted in too few events in the severe outcome groups within age categories. In contrast, the low RoB study by Tseng et al. 2020 [12] found significantly higher odds of death within one year post admission among older hospitalised patients. The study reported an adjusted odds ratio (aOR) of 5.37 (95% CI: 1.32-22.90) for adults aged 75-84 and 5.12 (95% CI: 1.17-22.40) for adults ≥ 85 years compared with younger adults (60-64 years), after adjusting for potential confounding factors. The same study also examined death within 60 days of admission and observed a trend of increasing risk with age in both crude and adjusted analyses; however, this association was only statistically significant for those aged ≥ 85 years in crude analysis and not after adjustment.

When the outcome was hospitalisation versus non hospitalisation, the medium RoB study by Shubert et al. 2021 reported an OR of 5.25 (95% CI: 2.2-12.5) for adults > 65 when compared to adults ≤ 65 years old. No adjusted analysis was reported.

Interpretation

The evidence on age as a risk factor for severe RSV outcomes is mixed. While one low RoB study suggests a strong to very strong association with advancing age, several studies, including others with low risk of bias, found no statistically significant association. Where associations were observed, they were not always robust to adjustment for confounders and were often imprecise, with wide confidence intervals and small numbers of events. In addition, the evidence base is limited to a small number of studies, further reducing confidence in the consistency and strength of the association.

Table 5. Age

Author, year	Global risk of bias	Study population + Mean age	Outcome comparison				Clinical risk factor	Crude effect estimate (RR, OR, HR)	Adjusted effect estimate			
			Severe	Sample size	Less severe	Sample size			(aRR, aOR, aHR)	Adjustment factors		
Goldman, 2022 [10]	Low	Adults ≥18 years Median age 69 years (IQR: 57-82)	Severe outcomes (ICU, mechanical ventilation, death)	77	Hospitalisation	326	Categorised	OR (95% CI)*	aOR (95% CI):	Sex, comorbid conditions		
							18-49 years				1.73 (0.75-4.00)	
							50-64 years				Reference group	
							65-79 years				1.76 (0.86-2.61)	
							≥80 years				1.25 (0.58-2.70)	
Tseng, 2020 [12]	Low	Adults ≥60 years Median age 78 years (range: 60-103)	Death (short-term ≤60 days)	75	Survival up to 60 days	627	Categorised	HR (95% CI):	aHR (95% CI):	Sex, prior hospitalisations, tachypnoea, altered level of consciousness, lymphoma, community-acquired pneumonia, acute renal failure, atrial fibrillation, neurovascular complication, nasal congestion, chills.		
							60-64 years				Reference group	Reference group
							65-74 years				1.18 (0.33-4.22)	1.51 (0.40-5.64)
							75-84 years				2.32 (0.71-7.66)	2.48 (0.73-8.49)
							≥85 years				3.49 (1.07-11.4)	2.79 (0.83-9.35)
			Death (long-term 1-365 days)	171	Survival up to 1 year	493	60-64 years	Reference group	Reference group			
							65-74 years	3.53 (0.83-15.00)	3.30 (0.75-14.60)			
							75-84 years	5.52 (1.33-22.90)	5.37 (1.32-22.90)			
							≥85 years	6.17 (1.49-25.70)	5.12 (1.17-22.40)			
Boattini, 2023 [15]	Medium	Adults ≥18 years Mean age: 71.2 years (SD 16,9)	Death	10	Hospitalisation	64	Continuous	OR (95% CI): 0.98 (0.94-1.02)	aOR (95% CI): 0.97 (0.93-1.02)	Sex, non-invasive ventilation		
											Boattini, 2021 [14]	Medium
Schubert, 2021 [13]	Medium	Adults (age range not specified)	Hospitalisation	45	No hospitalisation	58	Categorised >65 years vs. ≤65 years	OR (95% CI): 5.25 (2.2-12.5)				

Author, year	Global risk of bias	Study population + Mean age	Outcome comparison				Clinical risk factor	Crude effect estimate (RR, OR, HR)	Adjusted effect estimate	
			Severe	Sample size	Less severe	Sample size			(aRR, aOR, aHR)	Adjustment factors
		Median age 57 years (IQR: 40-73)	ICU	7	Hospitalisation	45	>65 years vs. ≤65 years	2.43 (0.51-11.51)		
			Death	3	Hospitalisation	45	>65 years vs. ≤65 years	1.13 (1-12.74)		
Walsh, 2013 [18]	High	Adults ≥21 years Hospitalisation group: mean age 70.5 years (SD: 147) No hospitalisation group: mean age 56,7 years (SD: 17,1)	Hospitalisation	50	No hospitalisation	61	Categorised per 10-year increase	OR (95% CI): 1.4 (0.96-2.1)		

Intensive care unit (ICU); odds ratio (OR); adjusted odds ratio (aOR); hazard ratio (HR); adjusted hazard ratio (aHR)

** Crude effect measures were also presented, but as the reference group was not specified, only the adjusted effect measures are shown.*

Sex

A total of six studies evaluated the association between sex and severe RSV disease in adults. Of these, three were assessed as having low RoB, two as medium, and one as high. Most studies were hospital-based cohorts or retrospective database analyses conducted in high-income countries between 2005 and 2008 and 2010 and 2022. The outcome comparison was either hospitalisation versus no hospitalisation or hospitalisation versus more severe outcome.

Table 6 summarises the findings of included studies assessing sex as a risk factor for severe RSV outcomes, by RoB, comparison group, and publication year.

Description of evidence

Among the low RoB studies, sex was not identified as a risk factor associated with any severe outcome. Among the medium RoB studies, a single small-cohort study by Boattini et al. 2021 [14] reported higher odds of death among men when death was compared to hospitalisation (aOR 3.30 (95% CI: 1.07-10.10)), adjusting for age. The high RoB study by Walsh et al. 2013 [18] reported higher odds of hospitalisation among women compared with men (OR 5.4 (95% CI: 1.2-23.8)). However, Walsh et al. 2013 [18] made a calculation error, stating that 33% of the outpatients are male. This is incorrect, as 24 out of 61 outpatients are noted as male (39%). If "33% male" was a typographical error, the results are unaffected. However, if that incorrect proportion reflects what was used in the analysis dataset, the female sex effect may have been overestimated in the multivariate model and would likely become non-significant when corrected.

Interpretation

The most robust evidence from low RoB studies did not find sex to be associated with a risk of more severe RSV infection outcome. One medium RoB study reported a strong association between male sex and mortality, however, this estimate was based on a small sample. A high RoB study also reported an association for female sex, but concerns regarding data accuracy limit confidence in this finding. Overall, the available evidence does not support sex as an independent risk factor for severe RSV disease in adults associated in the hospital setting.

Pregnancy

None of the included studies evaluated pregnancy as a potential risk factor for severe RSV outcomes in the mother.

Table 6. Sex

Author, year	Global risk of bias	Study population + Mean age	Outcome comparison				Clinical risk factor	Crude effect estimate (RR, OR, HR)	Adjusted effect estimate	
			Severe	Sample size	Less severe	Sample size			(aRR, aOR, aHR)	Adjustment factors
Haeberer, 2024 [16]	Low	Adults ≥60 years	Hospitalisation	635	No hospitalisation	71	Male		aOR (95% CI): 1.42 (0.83-2.45)	Specific adjustment factors not reported
Goldman, 2022 [10]	Low	Adults ≥18 years Median age 69 years (IQR: 57-82)	Severe outcomes (ICU, mechanical ventilation, death)	77	Hospitalisation	326	Female	OR (95% CI): 0.83 (0.50-1.37)		Age, comorbid conditions
							Male		aOR (95% CI): 1.20 (0.70-2.07)	
Tseng, 2020 [12]	Low	Adults ≥60 years Median age 78 years (range: 60-103)	Death (short-term ≤60 days)	75	Survival up to 60 days	627	Female	HR (95% CI): 0.88 (0.55-1.38)	aHR (95% CI): 1.05 (0.64-1.70)	Age, prior hospitalisations, tachypnoea, altered level of consciousness, lymphoma, community-acquired pneumonia, acute renal failure, atrial fibrillation, neurovascular complication, nasal congestion, chills.
			Death (long-term 1-365 days)	171	Survival up to 1 year	1493	Female	HR (95% CI): 0.73 (0.49-1.09)	aHR (95% CI): 0.69 (0.46-1.05)	Sex, prior hospitalisations, weakness, lymphoma, dementia, end stage renal disease, chronic heart failure, exacerbation, cough, vomiting, dizziness.
Boattini, 2023 [15]	Medium	Adults ≥18 years Mean age: 71.2 years (SD 16,9)	Death	10	Hospitalisation	64	Male	OR (95% CI): 2.19 (0.56-8.54)		
Boattini, 2021 [14]	Medium	Adults ≥65 years Mean age 80.9 years (SD: 8,7)	Death	20	Hospitalisation	146	Male		aOR (95% CI): 3.30 (1.07-10.10)	Age
Walsh, 2013 [18]	High	Adults ≥21 years	Hospitalisation	50	No hospitalisation	61	Female		aOR (95% CI): 5.4 (1.2-23.8)	

Author, year	Global risk of bias	Study population + Mean age	Outcome comparison				Clinical risk factor	Crude effect estimate	Adjusted effect estimate	
			Severe	Sample size	Less severe	Sample size		(RR, OR, HR)	(aRR, aOR, aHR)	Adjustment factors
		Hospitalisation group: mean age 70.5 years (SD: 147) No hospitalisation group: mean age 56,7 years (SD: 17,1)								

Intensive care unit (ICU); odds ratio (OR); adjusted odds ratio (aOR); hazard ratio (HR); adjusted hazard ratio (aHR)

3.3.2 Comorbidity factors

Lung disease

A total of seven studies evaluated the association between lung disease and severe RSV disease in adults. Of these, three were assessed as having low RoB, three as medium, and one as high. Most studies were hospital-based cohorts or retrospective database analyses conducted in high-income countries between 2005 and 2008 and 2010 and 2024. The outcome comparison was either hospitalisation versus no hospitalisation or hospitalisation versus more severe outcome.

Table 7 summarises the findings of included studies assessing lung disease as a risk factor for severe RSV outcomes, by RoB, comparison group, and publication year.

Description of evidence

Across the low RoB studies, lung disease, and particularly chronic obstructive pulmonary disease (COPD), was identified as a risk factor for severe RSV infection, however, these findings were primarily based on crude estimates. Ma et al. 2025 reported an RR of 2.14 (95% CI: 1.52-3.00) and 2.21 (95% CI: 1.60-3.07) for the age-groups 18-59 years and ≥ 60 years, respectively, when comparing hospitalisation versus ICU, organ failure or death. Similarly, Goldman et al. 2022 [10] reported an OR of 1.75 (95% CI: 1.01-3.04) for COPD; however, adjusted analyses were only reported for broader respiratory conditions and did not identify an association.

Haerberer et al. 2024 [16], also a low RoB study, found chronic lung disease to be associated with hospitalisation in an adjusted analyses (aOR 1.93 (95% CI: 1.11-3.38)) but not with more severe outcome (ICU, death etc.) among hospitalised patients.

Among the medium RoB studies, Schubert et al. 2021 [13] identified COPD as a risk factor for hospitalisation (OR 3.35 (95% CI: 1.41-7.96)), and reported respiratory illness as associated with ICU admission in an already hospitalised cohort (OR 6.07 (95% CI: 1.11-33.16)), however these estimates were also based on crude analyses.

The high RoB study by Joseph et al. 2025 [11] did not identify any chronic lung diseases as risk factors in a smaller hospitalised cohort, when adjusting for age and sex.

Except for Boattini et al. 2021 [14], which reported sleep apnoea as a clinical risk factor (aOR 8.39 (95% CI: 2.14-32.89)), other specific chronic lung conditions such as asthma were not identified as risk factors in other studies investigating these comorbidities.

Interpretation

Overall, COPD appears to be associated with an increased risk of hospitalisation, with moderate to strong effect estimates observed in some studies. However, these estimates are largely based on crude analyses, with limited adjustment for key confounders such as age. Evidence for an association between COPD or chronic lung disease and more severe outcomes, such as ICU admission or death, is inconsistent across studies. Although some findings suggest an increased risk of severe outcomes, the available estimates are often imprecise and not consistently adjusted for confounding. Variation in findings may also reflect small cohort sizes and differences in outcome definitions beyond hospital admission. Overall, the evidence remains mixed and context dependent and does not allow for firm conclusions regarding the independent effect of COPD on severe RSV outcomes.

Table 7. Lung disease

Author, year	Global risk of bias	Study population + Mean age	Outcome comparison				Clinical risk factor	Crude effect estimate (RR, OR, HR)	Adjusted effect estimate	
			Severe	Sample size	Less severe	Sample size			(aRR, aOR, aHR)	Adjustment factors
Ma, 2025 [17]	Low	Adults ≥18 years Median age 66 years (IQR: 54-75)	ICU, organ failure, death	Aged 18-59 years: 96	Hospitalisation	301	COPD	RR (95% CI): 2.14 (1.52-3.00)		
				Aged ≥60 years: 164	Hospitalisation	550	COPD	RR (95% CI): 2.21 (1.60-3.07)		
Haeberer, 2024 [16]	Low	Adults ≥60 years	Hospitalisation	635	No hospitalisation	71	Chronic lung disease		aOR (95% CI): 1.93 (1.11-3.38)	Specific adjustment factors not reported
		Hospitalised group: mean age 79.5 years (SD 9,4) No mean age reported for severe outcome group	Severe (ICU, death, prolonged hospital stay, or hospital readmission after discharge)	Composite number not reported	Less severe (no ICU, no death, no prolonged hospital stay, no readmission)	635	Chronic lung disease		aOR (95% CI): 1.00 (0.78-1.46)	
Goldman, 2022 [10]	Low	Adults ≥18 years Median age 69 years (IQR: 57-82)	Severe outcomes (ICU, mechanical ventilation, death)	77	Hospitalisation	326	Any respiratory condition	OR (95% CI): 1.19 (0.72-1.95)	aOR (95% CI): 1.36 (0.80-2.33)	Age, sex
							COPD	OR (95% CI): 1.75 (1.01-3.04)		
							Asthma	OR (95% CI): 1.12 (0.64-1.95)		
Boattini, 2023 [15]	Medium	Adults ≥18 years Mean age: 71.2 years (SD 16,9)	Death	10	Hospitalisation	64	COPD/asthma	OR (95% CI): 1.78 (0.46-6.81)		
							Obstructive sleep apnoea/obesity hypoventilation system	OR (95% CI): 1.66 (0.16-16.63)		
Boattini, 2021 [14]	Medium	Adults ≥65 years Mean age 80.9 years (SD: 8,7)	Death	20	Hospitalisation	146	Obstructive sleep apnoea/obesity hypoventilation system		aOR (95% CI): 8.39 (2.14-32.89)	Age, sex
Schubert, 2021 [13]	Medium	Adults (age range not specified)	Hospitalisation	45	No hospitalisation	58	Respiratory illness	OR (95% CI): 3.35 (1.41-7.96)		
			ICU	7	Hospitalisation	45	Respiratory illness	OR (95% CI):		

Author, year	Global risk of bias	Study population + Mean age	Outcome comparison				Clinical risk factor	Crude effect estimate (RR, OR, HR)	Adjusted effect estimate	
			Severe	Sample size	Less severe	Sample size			(aRR, aOR, aHR)	Adjustment factors
		Median age 57 years (IQR: 40-73)	Death	3	Hospitalisation	45	Respiratory illness	6.07 (1.11-33.16) OR (95% CI): 4.45 (0.39-50.95)		
Joseph, 2025 [11]	High	Adults ≥18 years Median age: 79 years (IQR 66-81)	Severe composite outcome (ICU and death)	25	Hospitalisation	111	COPD		aOR (95% CI): 0.75 (0.25-2.29)	Age, sex
							Asthma		aOR (95% CI): 1.05 (0.27-4.11)	
			ICU	19	Hospitalisation	111	COPD		aOR (95% CI): 2.31 (0.74-7.18)	
							Asthma		aOR (95% CI): 0.78 (0.15-4.08)	
			Death	9	Hospitalisation	111	COPD		aOR (95% CI): 0.82 (0.09-7.41)	
							Asthma		aOR (95% CI): 4.15 (0.64-27.03)	

Intensive care unit (ICU); risk ratio (RR); adjusted risk ratio (aRR); odds ratio (OR); adjusted odds ratio (aOR)

* Including asthma, chronic obstructive pulmonary disease, sleep apnoea, cystic fibrosis, interstitial lung disease, bronchiectasis, pulmonary fibrosis, and/or pulmonary hypertension

Cardiovascular and cerebrovascular disease

A total of six studies evaluated the association between cardiovascular and cerebrovascular disease and severe RSV disease in adults. Of these, three were assessed as having low RoB studies, two as medium, and one as high. Most studies were hospital-based cohorts or retrospective database analyses conducted in high-income countries between 2010 and 2024. The outcome comparison was either hospitalisation versus no hospitalisation or hospitalisation versus more severe outcome.

Table 8 summarises the findings of included studies assessing cardiovascular and cerebrovascular diseases as risk factors for severe RSV outcomes, by RoB, comparison group, and publication year.

Description of evidence

Whether cardiovascular and cerebrovascular diseases were identified as risk factors varied across all studies, regardless of RoB scores. The low RoB study by Haeberer et al. 2024 [16] reported an aOR of 3.79 (95% CI: 2.17-6.62) for cardiovascular and cerebrovascular disease in general for hospitalised patients compared to no hospitalisation. Tseng et al. 2020 [12] also a low RoB study, reported an aHR of 1.86 (95% CI: 1.11-3.13) for congestive heart failure associated with all-cause death up to one year after hospitalisation. This study included the largest cohort comprising 664 patients; however, the outcome measure was broad, and its follow-up period extended, reflecting a cohort of frail, elderly hospitalised patients. Consequently, the findings may not be generalisable to broader adult populations, as it is unclear whether the identified factors reflect general predictors of mortality in older adults rather than RSV-specific effects. In addition, a proportion of infections was confirmed by viral culture, which has lower sensitivity and specificity than PCR and requires higher viral loads. The authors do not report how RSV positivity was verified or how many samples were tested, raising concerns about specificity, potential false negatives, and incomplete case ascertainment. These uncertainties, together with the narrow study population, indicate that the findings should be interpreted with caution, despite the study's low RoB.

The remaining low RoB study by Goldman et al. 2022 [10] did not identify cardiovascular and cerebrovascular diseases as significant risk factors for an outcome more severe than hospitalisation (aOR 0.73 (95% CI: 0.42-1.27)).

Among the medium RoB studies, only Schubert et al. 2021 [13] identified cardiac illness as a risk factor associated with hospitalisation (OR 4.03 (95% CI: 1.75-9.28)), though this was based on crude estimates.

Interpretation

Overall, cardiovascular and cerebrovascular disease appear to be associated with an increased risk of hospitalisation, with moderate to strong effect estimates observed in some studies. However, the evidence for an association with more severe disease outcome, such as ICU admission or death, is inconsistent across studies. Although there is some indication of increased risk of severe outcomes, the available estimates are not always based on adjusted analyses. Overall, the evidence remains mixed and context dependent and does not allow for firm conclusions.

Table 8. Cardiovascular and cerebrovascular disease

Author, year	Global risk of bias	Study population + Mean age	Outcome comparison				Clinical risk factor	Crude effect estimate	Adjusted effect estimate	
			Severe	Sample size	Less severe	Sample size		(RR, OR, HR)	(aRR, aOR, aHR)	Adjustment factors
Goldman, 2022 [10]	Low	Adults ≥18 years Median age 69 years (IQR: 57-82)	Severe outcomes (ICU, mechanical ventilation, death)	77	Hospitalisation	326	Any cardiac conditions	OR (95% CI): 0.79 (0.48-1.30)	aOR (95% CI): 0.73 (0.42-1.27)	Age, sex
							Congestive heart failure	OR (95% CI): 1.15 (0.67-1.99)		
Haeberer, 2024 [16]	Low	Adults ≥60 years Hospitalised group: mean age 79.5 years (SD 9,4) No mean age reported for the severe outcome group	Hospitalisation	635	No hospitalisation	71	Cardiovascular or cerebrovascular disease		aOR (95% CI): 3.79 (2.17-6.62) aOR (95% CI): 1.18 (0.76-1.84)	Adjustment factors not reported
							Cardiovascular or cerebrovascular disease			
Tseng, 2020 [12]	Low	Adults ≥60 years Median age 78 years (range: 60-103)	Death (long-term 1-365 days)	171	Survival up to 1 year	493	Congestive heart failure	HR (95% CI): 2.46 (1.50-4.04)	aHR (95% CI): 1.86 (1.11-3.13)	Sex, prior hospitalisations, weakness, lymphoma, dementia, end stage renal disease, chronic heart failure, exacerbation, cough, vomiting, dizziness.
Boattini, 2023 [15]	Medium	Adults ≥18 years Mean age: 71.2 years (SD 16,9)	Death	10	Hospitalisation	64	Chronic heart failure	OR (95% CI): 2.00 (0.50-8.00)		
Schubert, 2021 [13]	Medium	Adults (age range not specified) Median age 57 years (IQR: 40-73)	Hospitalisation	45	No hospitalisation	58	Cardiac illness	OR (95% CI): 4.03 (1.75-9.28)		
			ICU	7	Hospitalisation	45	Cardiac illness	OR (95% CI): 6 (0.7-51.74)		
			Death	3	Hospitalisation	45	Cardiac illness	OR (95% CI): 1.85 (0.16-21.02)		
Joseph, 2025 [11]	High	Adults ≥18 years Median age: 79 years (IQR 66-81)	Severe composite outcome (ICU and death)	25	Hospitalisation	111	Coronary artery disease or myocardial infarction		aOR (95% CI): 2.37 (0.86-6.53)	Age, sex
							Peripheral arterial disease		aOR (95% CI): 0.81 (0.16-4.02)	
							Stroke or transient ischaemic attack		aOR (95% CI): 0.87 (0.27-2.83)	
							Arrhythmia		aOR (95% CI):	

Author, year	Global risk of bias	Study population + Mean age	Outcome comparison				Clinical risk factor	Crude effect estimate (RR, OR, HR)	Adjusted effect estimate	
			Severe	Sample size	Less severe	Sample size			(aRR, aOR, aHR)	Adjustment factors
			ICU	19	Hospitalisation	111	Coronary artery disease or myocardial infarction		0.75 (0.25-2.29)	
						Peripheral arterial disease		aOR (95% CI): 2.33 (0.70-7.69)		
						Stroke or transient ischaemic attack		aOR (95% CI): 0.46 (0.05-3.92)		
						Arrhythmia		aOR (95% CI): 0.86 (0.22-3.35)		
			Death	9	Hospitalisation	111	Coronary artery disease or myocardial infarction		aOR (95% CI): 1.16 (0.32-4.18)	
						Peripheral arterial disease		aOR (95% CI): 2.82 (0.62-12.75)		
						Stroke or transient ischaemic attack		aOR (95% CI): 1.60 (0.17-15.06)		
						Arrhythmia		aOR (95% CI): 1.44 (0.27-7.73)		
								aOR (95% CI): 0.89 (0.19-4.14)		

Intensive care unit (ICU); odds ratio (OR); adjusted odds ratio (aOR); hazard ratio (HR); adjusted hazard ratio (aHR)

Diabetes

Three studies evaluated the association between diabetes and severe RSV disease in adults. Of these, two were assessed as having medium RoB, and one as high. Most studies were hospital-based cohorts or retrospective database analyses conducted in high-income countries between 2017 and 2019 and 2022 and 2024. The outcome comparison was either hospitalisation versus no hospitalisation or hospitalisation versus more severe outcome.

Table 9 summarises the findings of included studies assessing diabetes as a risk factor for severe RSV outcomes, by RoB, comparison group, and publication year.

Description of evidence

Evidence for diabetes as a risk factor associated with severe outcomes was not evident across the included studies. The medium RoB study by Schubert et al. 2021 [13] reported type II diabetes as a risk factor associated with hospitalisation with an OR of 2.96 (95% CI: 1.07-8.21), although this was based on crude estimates. The high RoB study by Joseph et al. 2025 [11] provided adjusted effect estimates but did not identify an association.

Interpretation

Findings across studies investigating diabetes as a risk factor for severe RSV infection were inconsistent. Overall, it remains unclear whether diabetes is associated with severe disease outcomes, as the available evidence is limited, based primarily on crude estimates, and does not allow for firm conclusions.

Table 9. Diabetes

Author, year	Global risk of bias	Study population + Mean age	Outcome comparison				Clinical risk factor	Crude effect estimate (RR, OR, HR)	Adjusted effect estimate	
			Severe	Sample size	Less severe	Sample size			(aRR, aOR, aHR)	Adjustment factors
Boattini, 2023 [15]	Medium	Adults ≥18 years Mean age: 71.2 years (SD 16,9)	Death	10	Hospitalisation	64	Diabetes	OR (95% CI): 0.28 (0.03-2.40)		
Schubert, 2021 [13]	Medium	Adults (age range not specified) Median age 57 years (IQR: 40-73)	Hospitalisation	45	No hospitalisation	58	Diabetes type II	OR (95% CI): 2.96 (1.07-8.21)		
			ICU	7	Hospitalisation	45	Diabetes type II	OR (95% CI): 1.73 (0.31-9.66)		
			Death	3	Hospitalisation	45	Diabetes type II	OR (95% CI): 9.11 (0.78-106.01)		
Joseph, 2025 [11]	High	Adults ≥18 years Median age: 79 years (IQR 66-81)	Severe composite outcome (ICU and death)	25	Hospitalisation	111	Diabetes		aOR (95% CI): 0.41 (0.11-1.52)	Age, sex
			ICU	19	Hospitalisation	111	Diabetes		aOR (95% CI): 0.49 (0.13-1.94)	
			Death	9	Hospitalisation	111	Diabetes		aOR (95% CI): 0.66 (0.07-6.17)	

Intensive care unit (ICU); odds ratio (OR); adjusted odds ratio (aOR).

Kidney disease

Five studies evaluated the association between kidney disease and severe RSV infection in adults. Of these, two were assessed as having low RoB, two as medium, and one as high. Most studies were hospital-based cohorts or retrospective database analyses conducted in high-income countries between 2010 and 2024. The outcome comparison was either hospitalisation versus no hospitalisation or hospitalisation versus more severe outcome.

Table 10 summarises the findings of included studies assessing kidney disease as a risk factor for severe RSV outcomes, by RoB, comparison group, and publication year.

Description of evidence

One of the two low RoB studies reported kidney disease as a risk factor associated with mortality in an already hospitalised group. Tseng et al. 2020 [12] reported an aHR of 2.13 (95% CI: 1.08-4.17) for end-stage renal disease when assessing long-term death (up to one year) in a hospitalised group, adjusting for potential confounding factors. In contrast another low RoB study, Haeberer et al. 2024 [16], did not identify an association between kidney disease and either hospitalisation or more severe outcomes.

Among the medium RoB studies, Schubert et al. 2021 [13] found an almost statistically significant estimate for dialysis and hospitalisation (OR 3.38 (95% CI: 0.97-11.79), although this was based on crude estimates. Estimates for ICU admission and death in the same study were difficult to interpret given the small sample sizes and unusually narrow confidence intervals. The remaining medium RoB study (Boattini et al. 2023, [15]) did not identify an association between chronic kidney disease and death. Notably, the low RoB study assessed long-term mortality up to one year after hospitalisation, whereas the medium RoB studies assessed in-hospital outcomes.

The high RoB study by Joseph et al. 2025 [11] reported higher adjusted odds of severe RSV disease outcomes among hospitalised adults with chronic kidney disease (aOR 2.64 (95% CI: 1.02-6.81)) and for death (aOR 11.63 (95% CI: 1.36-99.74)), however these estimates were based on a small sample with wide confidence intervals.

Interpretation

Based on the low RoB evidence, kidney disease may be a risk factor associated with long-term mortality after hospitalisation in an older population, with a moderate effect estimate observed in one study. However, this finding is not consistent across studies, particularly those assessing in-hospital outcomes. Overall, the evidence is limited and heterogeneous and does not allow for firm conclusions regarding kidney disease as an independent risk factor for severe RSV outcomes.

Table 10. Kidney disease

Author, year	Global risk of bias	Study population + Mean age	Outcome comparison				Clinical risk factor	Crude effect estimate (RR, OR, HR)	Adjusted effect estimate	
			Severe	Sample size	Less severe	Sample size			(aRR, aOR, aHR)	Adjustment factors
Haeberer, 2024 [16]	Low	Adults ≥60 years	Hospitalisation	635	No hospitalisation	71	Kidney disease		aOR (95% CI): 1.09 (0.45-2.63)	Adjustment factors not reported
		Hospitalised group: mean age 79.5 years (SD 9,4) No mean age reported for the severe outcome group	Severe (ICU, death, prolonged hospital stay, or hospital readmission after discharge)	Composite number not reported	Less severe (no ICU, no death, no prolonged hospital stay, no readmission)	635	Kidney disease		aOR (95% CI): 1.16 (0.75-1.17)	
Tseng, 2020 [12]	Low	Adults ≥60 years Median age 78 years (range: 60-103)	Death (long-term 1-365 days)	171	Survival up to 1 year	493	End-stage renal disease	HR (95% CI): 2.37 (1.30-4.35)	aHR (95% CI): 2.13 (1.08-4.17)	Age, sex, prior hospitalisations, weakness, lymphoma, dementia, end stage renal disease, chronic heart failure, exacerbation, cough, vomiting, dizziness.
Boattini, 2023 [15]	Medium	Adults ≥18 years Mean age: 71.2 years (SD 16,9)	Death	10	Hospitalisation	64	Chronic kidney disease	OR (95% CI): 0.69 (0.13-3.58)		
Schubert, 2021 [13]	Medium	Adults (age range not specified) Median age 57 years (IQR: 40-73)	Hospitalisation	45	No hospitalisation	58	Dialysis	OR (95% CI): 3.38 (0.97-11.79)		
			ICU	7	Hospitalisation	45	Dialysis	OR (95% CI): 0.87 (0.8-0.94)		
			Death	3	Hospitalisation	45	Dialysis	OR (95% CI): 0.87 (0.81-0.94)		
Joseph, 2025 [11]	High	Adults ≥18 years Median age: 79 years (IQR 66-81)	Severe composite outcome (ICU and death)	25	Hospitalisation	111	Chronic kidney disease		aOR (95% CI): 2.64 (1.02-6.81)	Age, sex
			ICU	19	Hospitalisation	111	Chronic kidney disease		aOR (95% CI): 2.05 (0.68-6.21)	
			Death	9	Hospitalisation	111	Chronic kidney disease		aOR (95% CI): 11.63 (1.36-99.74)	

Intensive care unit (ICU); odds ratio (OR); adjusted odds ratio (aOR); hazard ratio (HR); adjusted hazard ratio (aHR)

Liver disease

Two studies evaluated the association between liver disease and severe RSV infection in adults. Of these, one was assessed as having low RoB study and one as high. The studies were both retrospective hospital-based cohort studies conducted in high-income countries between 2010 and 2024. The outcome comparison was either hospitalisation versus no hospitalisation or hospitalisation versus more severe outcome.

Table 11 summarises the findings of included studies assessing liver disease as a risk factor for severe RSV outcomes, by RoB, comparison group, and publication year.

Description of evidence

Neither study found an association between liver disease and hospitalisation or more severe outcomes (ICU admission, prolonged stay, death, etc.). However, the study cohorts were small and, in the low RoB study, composite outcome counts were not reported. Furthermore, the high RoB study by Joseph et al. 2025 [11] showed some inconsistencies in reporting between the text and tables. Thus, in addition to the small study cohort, the results from this study should be interpreted with caution.

Interpretation

Based on the two included studies, it remains unclear whether liver disease is associated with severe RSV infection in adults. The available evidence is limited, based on small sample sizes and a single low RoB study, and does not allow for firm conclusions.

Table 11. Liver disease

Author, year	Global risk of bias	Study population + Mean age	Outcome comparison				Clinical risk factor	Crude effect estimate (RR, OR, HR)	Adjusted effect estimate	
			Severe	Sample size	Less severe	Sample size			(aRR, aOR, aHR)	Adjustment factors
Haebeler, 2024 [16]	Low	Adults ≥60 years	Hospitalisation	635	No hospitalisation	71	Liver disease		aOR (95% CI): 5.05 (0.83-30.6)	Adjustment factors not reported
		Hospitalised group: mean age 79.5 years (SD 9,4) No mean age reported for the severe outcome group	Severe (ICU, death, prolonged hospital stay, or hospital readmission after discharge)	Composite number not reported	Less severe (no ICU, no death, no prolonged hospital stay, no readmission)	635	Liver disease		aOR (95% CI): 1.27 (0.70-2.28)	
Joseph, 2025 [11]	High	Adults ≥18 years	Severe composite outcome (ICU and death)	25	Hospitalisation	111	Chronic liver disease		aOR (95% CI): 1.43 (0.35-5.81)	Age, sex
		Median age: 79 years (IQR 66-81)	ICU	19	Hospitalisation	111	Chronic liver disease		aOR (95% CI): 1.09 (0.21-5.75)	
		Death	9	Hospitalisation	111	Chronic liver disease		aOR (95% CI): 4.88 (0.76-31.36)		

Intensive care unit (ICU); adjusted odds ratio (aOR)

Neurological disease

Three studies evaluated the association between neurological disease and severe RSV infection in adults. All were assessed as having low RoB. The studies were hospital-based cohorts or retrospective database analyses conducted in high-income countries between 2010 and 2022. The outcome comparison was either hospitalisation versus no hospitalisation or hospitalisation versus more severe outcome.

Table 12 summarises the findings of included studies assessing neurological disease as a risk factor for severe RSV outcomes, by RoB, comparison group, and publication year.

Description of evidence

Two of the three studies identified neurological disease as a risk factor associated with severe outcomes. Haeberer et al. 2024 [16] found that neurologic condition was associated with hospitalisation (aOR 2.20 (95% CI: 1.09-4.46)), but not with more severe outcomes (ICU, prolonged hospital stay, death, etc.), in a cohort of adults ≥ 60 years, however adjustment factors were not reported. Tseng et al. 2020 [12] reported an aHR of 1.86 (95% CI: 1.08-3.19) for dementia associated with death up to one year after hospitalisation in adults ≥ 60 years, adjusting for potential confounding factors including age, sex, prior hospitalisation, and other comorbidities.

Goldman et al. 2022 [10] did not identify an association between neurological conditions and more severe outcomes in hospitalised adults ≥ 18 years.

Interpretation

There is some variation across the included studies regarding neurological disease as a risk factor for severe RSV infection. Two low RoB studies reported moderate associations with severe outcomes, whereas one study did not identify an association. Overall, the evidence suggests a possible increased risk of severe outcomes among adults with neurological disease, particularly in those aged ≥ 60 years; however, the findings are not fully consistent and do not allow for firm conclusions.

Table 12. Neurological disease

Author, year	Global risk of bias	Study population + Mean age	Outcome comparison				Clinical risk factor	Crude effect estimate (RR, OR, HR)	Adjusted effect estimate	
			Severe	Sample size	Less severe	Sample size			(aRR, aOR, aHR)	Adjustment factors
Haebeler, 2024 [16]	Low	Adults ≥60 years	Hospitalisation	635	No hospitalisation	71	Neurologic condition		aOR (95% CI): 2.20 (1.09-4.46)	Adjustment factors not reported
		Hospitalised group: mean age 79.5 years (SD 9,4) No mean age reported for the severe outcome group	Severe (ICU, death, prolonged hospital stay, or hospital readmission after discharge)	Composite number not reported	Less severe (no ICU, no death, no prolonged hospital stay, no readmission)	635	Neurologic condition		aOR (95% CI): 1.23 (0.85-1.76)	
Goldman, 2022 [10]	Low	Adults ≥18 years Median age 69 years (IQR: 57-82)	Severe outcomes (ICU, mechanical ventilation, death)	77	Hospitalisation	326	Any neurological conditions	OR (95% CI): 0.88 (0.50-1.54)	aOR (95% CI): 0.60 (0.30-1.18)	Age, sex
Tseng, 2020 [12]	Low	Adults ≥60 years Median age 78 years (range: 60-103)	Death (long-term 1-365 days)	171	Survival up to 1 year	493	Dementia	HR (95% CI): 2.12 (1.29-3.51)	aHR (95% CI): 1.86 (1.08-3.19)	Age, sex, prior hospitalisations, weakness, lymphoma, dementia, end stage renal disease, chronic heart failure, exacerbation, cough, vomiting, dizziness.

Intensive care unit (ICU); odds ratio (OR); adjusted odds ratio (aOR); hazard ratio (HR); adjusted hazard ratio (aHR)

Cancer or haematologic malignancies

Four studies evaluated the association between cancer and haematological disease and severe RSV infection in adults. Of these, one was assessed as having low RoB, two as medium and one as high. Most studies were hospital-based cohorts or retrospective database analyses conducted in high-income countries between 2011 and 2015, 2017 and 2019 and 2022 and 2024. The outcome comparison was either hospitalisation versus no hospitalisation or hospitalisation versus more severe outcome.

Table 13 summarises the findings of included studies assessing cancer or haematological disease as a risk factor for severe RSV outcomes, by RoB, comparison group, and publication year.

Description of evidence

The low RoB study by Tseng et al. 2020 [12] reported lymphoma as associated with all-cause death for both short-term (up to 60 days) (aHR 3.87 (95% CI 1.32-11.30)) and long-term (up to one year) (aHR 3.57 (95% CI 1.20-10.60)) periods, adjusting for potential confounding factors.

Among the medium RoB studies, Boattini et al. 2021 [14] reported a strong association between solid neoplasm and death (aOR 9.06 (95% CI: 2.44–33.54)); however, this estimate was based on a small sample and is imprecise. Schubert et al. 2021 [13] reported elevated crude, but non-significant, estimates for oncological illness across outcomes.

The high RoB study by Joseph et al. 2025 [11] investigated associations between chronic haematological disease and hospitalisation or more severe outcome in a small group of adults ≥ 18 years but found no associations.

Interpretation

Across the studies, cancer and haematological malignancies were associated with increased risk of death, with moderate to strong effect estimates observed in both low and medium RoB studies. However, these findings are based on a limited number of studies, and estimates, particularly from medium RoB studies, are often imprecise and based on small samples. In addition, as the low RoB study assessed all-cause mortality over extended follow-up periods and did not account for cancer severity, it remains unclear to what extent RSV infection contributed to the observed mortality.

Table 13. Cancer or haematological malignancies

Author, year	Global risk of bias	Study population + Mean age	Outcome comparison				Clinical risk factor	Crude effect estimate	Adjusted effect estimate	
			Severe	Sample size	Less severe	Sample size		(RR, OR, HR)	(aRR, aOR, aHR)	Adjustment factors
Tseng, 2020 [12]	Low	Adults ≥60 years Median age 78 years (range: 60-103)	Death (short-term ≤60 days)	75	Survival up to 60 days	627	Lymphoma	HR (95% CI): 2.81 (1.03-7.69)	aHR (95% CI): 3.87 (1.32-11.30)	Age, sex, prior hospitalisations, tachypnoea, altered level of consciousness, lymphoma, community-acquired pneumonia, acute renal failure, atrial fibrillation, neurovascular complication, nasal congestion, chills
			Death (long-term 1-365 days)	171	Survival up to 1 year	493	Lymphoma	HR (95% CI): 3.31 (1.21-9.00)	aHR (95% CI): 3.57 (1.20-10.60)	
Boattini, 2021 [14]	Medium	Adults ≥65 years Mean age 80.9 years (SD: 8,7)	Death	20	Hospitalisation	146	Solid neoplasm		aOR (95% CI): 9.06 (2.44-33.54)	
Schubert, 2021 [13]	Medium	Adults (age range not specified) Median age 57 years (IQR: 40-73)	Hospitalisation	45	No hospitalisation	58	Oncological illness (not defined)	OR (95% CI): 2.17 (0.86-5.49)		
			ICU	7	Hospitalisation	45	Oncological illness (not defined)	OR (95% CI): 2.68 (0.56-12.92)		
			Death	3	Hospitalisation	45	Oncological illness (not defined)	OR (95% CI): 7.09 (0.61-81.9)		
Joseph, 2025 [11]	High	Adults ≥18 years Median age: 79 years (IQR 66-81)	Severe composite outcome (ICU and death)	25	Hospitalisation	111	Chronic haematological disease (leukaemia and lymphoma)		aOR (95% CI): 1.38 (0.34-5.61)	Age, sex
			ICU	19	Hospitalisation	111	Chronic haematological disease (leukaemia and lymphoma)		aOR (95% CI): 0.49 (0.06-4.33)	
			Death	9	Hospitalisation	111	Chronic haematological disease (leukaemia and lymphoma)		aOR (95% CI): 2.19 (0.38-12.44)	

Hazard ratio (HR); adjusted hazard ratio (aHR); intensive care unit (ICU); adjusted odds ratio (aOR)

Other comorbidities

Two studies evaluated other comorbidities as potential risk factors for severe RSV infection in adults. One was assessed as having low RoB and one as medium. The outcome comparison was either hospitalisation versus no hospitalisation or hospitalisation versus more severe outcome.

Table 14 summarises the findings of included studies assessing other co-morbidities as risk factors for severe RSV outcomes, by RoB, comparison group, and publication year.

Description of evidence

The low RoB study by Haeberer et al. 2024 [16] did not identify an association between endocrine or metabolic disorders and either hospitalisation or more severe outcomes. Similarly, the medium RoB study by Schubert et al. 2021 [13] did not identify an association between solid organ transplant and severe RSV outcomes; however, estimates were based on crude analyses and were imprecise.

Interpretation

The available evidence on other comorbidities is limited and does not provide consistent evidence of an association with severe RSV outcomes. However, this is based on a small number of studies with imprecise estimates, and no firm conclusions can be drawn.

Table 14. Other comorbidities

Author, year	Global risk of bias	Study population + Mean age	Outcome comparison				Clinical risk factor	Crude effect estimate (RR, OR, HR)	Adjusted effect estimate	
			Severe	Sample size	Less severe	Sample size			(aRR, aOR, aHR)	Adjustment factors
Haeberer, 2024 [16]	Low	Adults ≥60 years	Hospitalisation	635	No hospitalisation	71	Endocrine or metabolic disorder	OR (95% CI): 1.09 (0.62-1.89)	aOR (95% CI): 1.08 (0.73-1.52)	Adjustment factors not reported
		Hospitalised group: mean age 79.5 years (SD 9,4) No mean age reported for the severe outcome group	Severe (ICU, death, prolonged hospital stay, or hospital readmission after discharge)	Compo site number not reported	Less severe (no ICU, no death, no prolonged hospital stay, no readmission)	635	Endocrine or metabolic disorder			
Schubert, 2021 [13]	Medium	Adults (age range not specified)	Hospitalisation	45	No hospitalisation	58	Solid organ transplant	OR (95% CI): 1.82 (0.66-5.02)		
		Median age 57 years (IQR: 40-73)	ICU	7	Hospitalisation	45	Solid organ transplant	OR (95% CI): 0.68 (0.08-5.97)		
			Death	3	Hospitalisation	45	Solid organ transplant	OR (95% CI): 0.8 (0.72-0.89)		

Intensive care unit (ICU); odds ratio (OR); adjusted odds ratio (aOR)

3.3.3 Immunosuppression

Three studies evaluated the association between immunosuppression and severe RSV infection in adults. Of these, two were assessed as having low RoB, and one as high. Most studies were hospital-based cohorts or retrospective database analyses conducted in high-income countries between 2010 and 2024. The outcome comparison was either hospitalisation versus no hospitalisation or hospitalisation versus more severe outcome. None of the included studies assessed the level or severity of immunosuppression, as most risk factors were analysed as binary variables, limiting evaluation of potential gradients of risk.

Table 15 summarises the findings of included studies assessing immunosuppression as a risk factor for severe RSV outcomes, by RoB, comparison group, and publication year.

Description of evidence

Among the low RoB studies, no statistical significance was reported for immunosuppression as a risk factor associated with more severe RSV outcomes in hospitalised cohorts. Haeberer et al. 2024 [16] also investigated immunocompromising conditions as potential risk factors for hospitalisation in adults ≥ 60 years but found no association. The high RoB study by Joseph et al. 2025 [11] reported higher odds of ICU admission among immunosuppressed patients (aOR 5.66 (95% CI: 1.02-6.81)), adjusting for sex and age.

Interpretation

The available evidence does not provide consistent evidence of an association between immunosuppression and severe RSV outcomes in adults. However, this conclusion is based on a limited number of studies, including one high RoB study reporting an association with ICU admission, and is constrained by small sample sizes and imprecise estimates.

Table 15. Immunosuppression

Author, year	Global risk of bias	Study population + Mean age	Outcome comparison				Clinical risk factor	Crude effect estimate	Adjusted effect estimate	
			Severe	Sample size	Less severe	Sample size		(RR, OR, HR)	(aRR, aOR, aHR)	Adjustment factors
Haebeler, 2024 [16]	Low	Adults ≥60 years	Hospitalisation	635	No hospitalisation	71	Immunocompromising condition (not specified)		aOR (95% CI): 0.86 (0.45-1.48)	Adjustment factors not reported
		Hospitalised group: mean age 79.5 years (SD 9,4) No mean age reported for the severe outcome group	Severe (ICU, death, prolonged hospital stay, or hospital readmission after discharge)	Composite number not reported	Less severe (no ICU, no death, no prolonged hospital stay, no readmission)	635	Immunocompromising condition (not specified)		aOR (95% CI): 1.01 (0.72-1.41)	
Goldman, 2022 [10]	Low	Adults ≥18 years Median age 69 years (IQR: 57-82)	Severe outcomes (ICU, mechanical ventilation, death)	77	Hospitalisation	326	Immunosuppressive conditions (not specified)	OR (95% CI): 0.89 (0.50-1.60)		
Joseph, 2025 [11]	High	Adults ≥18 years Median age: 79 years (IQR 66-81)	Severe composite outcome (ICU and death)	25	Hospitalisation	111	Immunosuppression*		aOR (95% CI): 2.98 (0.79-11.28)	Age, sex
			ICU	19	Hospitalisation	111	Immunosuppression*		aOR (95% CI): 5.66 (1.02-6.81)	
			Death	9	Hospitalisation	111	Immunosuppression*		aOR (95% CI): 1.48 (0.16-13.66)	

Intensive care unit (ICU); adjusted risk ratio (aRR)

** Specified as one or more of the following conditions: HIV/AIDS, history of organ transplantation, chemotherapy, prolonged corticosteroid use, or immunomodulating medications.*

3.3.4 Lifestyle factors

Smoking

Two studies evaluated the association between smoking and severe RSV infection in adults. Of these, one was assessed as having low RoB, and one as medium. Both studies were retrospective hospital-based cohorts studies conducted in high-income countries between 2010 and 2022. The outcome comparison was either hospitalisation versus no hospitalisation or hospitalisation versus more severe outcome.

Table 16 summarises the findings of included studies assessing smoking as a risk factor for severe RSV outcomes, by RoB, comparison group, and publication year.

Description of evidence

Haeberer et al. 2024 [16], a low RoB study, reported an adjusted OR of 2.81 (95% CI: 1.01-7.82) for previous smoking when hospitalisation was the outcome, however, the adjustment factors were not reported in the study.

Similarly, the medium RoB study by Schubert et al. 2021 [13] found smoking as a risk factor for hospitalisation when compared with no hospitalisation (OR 9.11 (95% CI: 4.3-24.39), though this was a crude estimate. Neither study identified smoking as associated with more severe outcomes in hospitalised cohorts.

Interpretation

Smoking may be associated with an increased risk of hospitalisation among adults with RSV infection, with moderate to strong effect estimates reported across the two included studies. However, the evidence is limited and includes both adjusted and crude estimates. No consistent association was observed for more severe outcomes, such as ICU admission or death. Overall, the available evidence suggests a possible association between smoking and hospitalisation but does not allow for firm conclusions.

Table 16. Smoking

Author, year	Global risk of bias	Study population + Mean age	Outcome comparison				Clinical risk factor	Crude effect estimate (RR, OR, HR)	Adjusted effect estimate	
			Severe	Sample size	Less severe	Sample size			(aRR, aOR, aHR)	Adjustment factors
Haeberer, 2024 [16]	Low	Adults ≥60 years Hospitalised group: mean age 79.5 years (SD 9,4) No mean age reported for the severe outcome group	Hospitalisation	635	No hospitalisation	71	Smoking - current		aOR (95% CI): 3.48 (0.95-12.8)	Adjustment factors not reported
							Smoking - previous		aOR (95% CI): 2.81 (1.01-7.82)	
			Severe (ICU, death, prolonged hospital stay, or hospital readmission after discharge)	Composite number not reported	Less severe (no ICU, no death, no prolonged hospital stay, no readmission)	635	Smoking - current		aOR (95% CI): 0.84 (0.36-1.95)	
							Smoking - previous		aOR (95% CI): 0.77 (0.39-1.55)	
Schubert, 2021 [13]	Medium	Adults (age range not specified) Median age 57 years (IQR: 40-73)	Hospitalisation	45	No hospitalisation	58	Smoking	OR (95% CI): 9.11 (3.4-24.38)		
			ICU	7	Hospitalisation	45	Smoking	OR (95% CI): 1.73 (0.36-8.24)		
			Death	3	Hospitalisation	45	Smoking	OR (95% CI): 1.11 (0.1-12.74)		

Intensive care unit (ICU); odds ratio (OR); adjusted odds ratio (aOR); hazard ratio (HR); adjusted hazard ratio (aHR)

Obesity

One low RoB study evaluated the association between weight and severe RSV infection in adults. This was a hospital-based retrospective database surveillance study conducted in the US with data collected in 2017-19. The outcome comparison was hospitalisation versus more severe outcome.

Table 17 summarises the findings from this study.

Description of evidence

The low RoB study by Goldman et al. 2022 [10] did not identify an association between obesity and more severe RSV outcomes in hospitalised adults (OR 0.68 (95% CI: 0.37-1.24)).

Interpretation

The available evidence on weight as a risk factor for severe RSV outcomes is limited to a single study and does not suggest an association.

Table 17. Obesity

Author, year	Global risk of bias	Study population + Mean age	Outcome comparison				Clinical risk factor	Crude effect estimate (RR, OR, HR)	Adjusted effect estimate	
			Severe	Sample size	Less severe	Sample size			(aRR, aOR, aHR)	Adjustment factors
Goldman, 2022 [10]	Low	Adults ≥18 years Median age 69 years (IQR: 57-82)	Severe outcomes (ICU, mechanical ventilation, death)	77	Hospitalisation	326	Obesity	OR (95% CI): 0.68 (0.37-1.24)		

Intensive care unit (ICU); Odds ratio (OR)

3.4 Meta-analysis

Among the nine articles, analyses and results were available across four different outcome groups including data from people with confirmed RSV: no hospitalisation vs. hospitalisation [13,16,18], hospitalisation vs. ICU admission [11,13,17], hospitalisation vs. composite severe outcomes [10,11,16], and hospitalisation vs. death [11-15].

- **No hospitalisation vs. hospitalisation:** None of the three studies that reported measures of association for clinical risk factors for RSV hospitalisation, reported clinical risk factors consistently enough across the studies to enable pooling of the data in a meta-analysis. The study populations differed with one including adults of ≥ 21 years and one which did not provide an age-cut off for their definition of adults. One study reported unadjusted odds ratios and one reported adjusted odds ratios from a multivariable logistic regression analysis. The definitions of clinical risk factors also varied, and several clinical risk factor categories had very small numbers. The small number of studies and substantial methodological heterogeneity precluded data pooling.
- **Hospitalisation vs. ICU admission:** Three studies compared hospitalised patients with those admitted to ICU. Study designs, populations, and analytical approaches differed considerably. Two studies reported unadjusted logistic regression and one adjusted logistic regression. Definitions of clinical risk factors and the extent of adjustment were not comparable, and outcome definitions varied. The small number of studies and substantial methodological heterogeneity precluded data pooling.
- **Hospitalisation vs. composite severe outcomes:** Three studies analysed composite "severe" outcomes, but the definitions differed (e.g. ICU admission, mechanical ventilation, and death; ICU admission and in-hospital death; or ICU admission in-hospital death, prolonged stay, or readmission). Analytical approaches also varied. Differences in study design, outcome definition, and analytical approach precluded data pooling.
- **Hospitalisation vs. death:** Five studies assessed mortality among hospitalised RSV cases. Study populations differed: two included adults aged ≥ 18 years, one included adults aged ≥ 60 years, one included adults aged ≥ 65 years, and one did not provide an age cut-off for their definition of adults. Mortality outcomes also varied (in-hospital, 30-day, 60-day, and one-year mortality), as did the effect measures (crude and adjusted HR, crude and adjusted OR). In several studies, both the total number of cases and the numbers within clinical risk factor subgroups were small, limiting statistical power and the reliability of estimated effects. When examining aggregate data to determine whether ORs could be calculated for studies that did not report them, this was not consistently possible. In addition, the definitions and categorisation of clinical risk factors varied. One study provided inconsistent numbers in the underlying raw data, affecting confidence in its reported effect estimates. On the basis of this evaluation, the between-study heterogeneity precluded data pooling.

Overall, the extent of heterogeneity in study populations, outcome and risk factor definitions, analytical methods, and reported effect measures rendered meta-analysis infeasible in this rapid review. Please see Tables 3 and 18 for further details.

Table 18. Feasibility of meta-analysis across outcome comparisons groups

Outcome group	No. of studies, authors, years and references	Outcome definitions	Study populations	Statistical methods/effect measures	Reporting of clinical risk factors	Comparability	Meta-analyses feasibility
No hospitalisation vs. hospitalisation	3 Schubert 2021, Haeberer 2024, Walsh 2013 [13,16,18]	Hospitalisation admission	Varying: Adults ≥ 18 years; ≥ 21 years; ≥ 60 years	Unadjusted and adjusted logistic regression (OR/aOR)	Variable definitions, very small subgroups (e.g. smoking)	Few studies, heterogeneous methods, exposures and effect measures	Not feasible
Hospitalisation vs. ICU admission	3 Joseph 2025, Schubert 2021, Ma 2025 [11,13,17]	ICU admission	Adults ≥ 18 years	Unadjusted and adjusted logistic regression (OR/aOR)	Limited data on clinical risk factors, unadjusted analyses, few variables assessed	Few studies, heterogeneous study designs, populations and analytical methods	Not feasible
Hospitalisation vs. composite severe outcomes	3 Goldman, 2022, Joseph 2025, Haeberer 2024 [10,11,16]	Different composite outcomes: ICU, mechanical ventilation, death; ICU, death during hospital stay, prolonged hospital stay, or hospital readmission after discharge; ICU, organ failure, death; ICU admission and/or in-hospital death	Varying: Adults ≥ 18 years; ≥ 60 years	Unadjusted and adjusted logistic regression (OR/aOR), Poisson regression (RR)	Differences in reported effect measures and included clinical risk factors	Few studies, different outcome definitions and analytical methods	Not feasible
Hospitalisation vs. death	5 Joseph 2025, Tseng 2020, Schubert 2021, Boattini 2021, Boattini 2023 [11-15]	Varying definitions: During admission, within 60 days post admission, 1-365 days post admission	Varying: Adults ≥ 18 years; ≥ 60 years; ≥ 65 years	Unadjusted and adjusted logistic regression (OR/aOR), Cox regression (HR/aHR)	Varying definitions and categorisation of clinical risk factors, small subgroup sizes	Heterogeneous populations, outcome definitions, statistical measures, and small numbers	Not feasible

4. Discussion

To improve understanding of populations at risk for severe RSV infection and guide targeted preventive interventions such as vaccination, this rapid systematic review aimed to identify clinical risk factors associated with hospitalisation, ICU admission, and death in adults following infection with RSV. In total, nine peer-reviewed papers were evaluated and included in this rapid review. Three of the included studies [13,16,18] investigated potential clinical risk factors associated with hospitalisation when compared to an outpatient RSV infected group. Five studies addressed clinical risk factors associated with a more severe outcome of RSV disease among already hospitalised patients; comparing hospitalisation with either ICU admission [11,13,17], or a composite of severe outcomes (including ICU admission, ventilation, prolonged hospital stay, readmission, or death) [10,11,16]. Five studies [11-15] addressed whether clinical risk factors were associated with mortality when compared to hospitalisation.

Main findings

Based on the included studies, this review identified some evidence that older age and chronic lung disease (particularly COPD) are associated with severe RSV outcomes in adults; however, these findings are based on a limited number of studies, are not consistently observed across all analyses, and are often derived from unadjusted or imprecise estimates. Neurological disease and cancer or haematological malignancies show similarly limited and uncertain evidence, with suggestive associations in some studies but comparable concerns regarding small sample sizes, wide confidence intervals and potential confounding. Evidence for cardiovascular disease is also uncertain and subject to the same methodological limitations and does not demonstrate a clearly stronger or more consistent association than other comorbidities.

Demographic factors

Age

Older age was one of the most consistently evaluated risk factor across the included studies and showed some of the strongest associations with severe RSV outcomes. In studies restricted to older populations (typically ≥ 60 or ≥ 65 years), some evidence suggested an increased risk with advancing age, particularly for mortality outcomes; however, this finding was primarily driven by a single low RoB study. Adjusted analyses from this study demonstrated moderate to very strong effect estimates, with the highest risks observed in the oldest age groups (e.g. ≥ 75 or ≥ 85 years).

However, findings were not consistent across all studies. Studies including broader adult populations (≥ 18 years) did not consistently identify an association, and some analyses based on crude estimates showed weaker or no clear effects. In addition, several studies were limited by small sample sizes and a low number of events, resulting in wide confidence intervals and reduced precision. While the magnitude of association in some adjusted analyses suggests a potentially strong independent effect of age, residual confounding by frailty and underlying health status may still contribute to the observed association.

Overall, the evidence indicates that older age is an important risk factor for severe RSV outcomes, particularly for mortality, although the strength and consistency of the association vary depending on study population, outcome definition, and adjustment for confounding factors.

Comorbidities

Lung disease

Lung disease, particularly COPD, was the most frequently evaluated risk factor across the included studies and showed a strong association with severe RSV infection. The magnitude of the crude effect was moderate to strong for the association between COPD and risk of hospitalisation, and one adjusted analysis from a low RoB study also reported an association with hospitalisation.

Furthermore, one low RoB study found COPD to be associated with outcomes more severe than hospitalisation (ICU, organ failure, death) in both age-groups (18-59 years and ≥ 60 years), based on crude estimates. However, the magnitude of association in adjusted analyses suggested only a limited to moderate association independent of age and sex. Whether the effect is independent of age remains unclear, as some attenuation after adjustment suggests partial confounding by age.

Overall, the evidence indicates that COPD is a clinical risk factor, particularly for hospitalisation; however, potential confounding factors obscure the strength of the association especially for an outcome more severe than hospitalisation. No association between severe RSV infection and other *specific* lung diseases was identified.

Cardiovascular and cerebrovascular disease

Cardiovascular and cerebrovascular diseases were evaluated in six studies and showed moderate to strong association with severe RSV outcomes; however, the consistency of findings across studies was mixed. Some evidence suggested an increased risk for hospitalisation, primarily based on an adjusted analysis from a single low RoB study.

Evidence for an association with more severe outcomes, particularly mortality, was limited and context-dependent, as this finding was based on a low RoB study including only frail, elderly, hospitalised patients. Whether the associations are independent of age is unclear, as the evidence is likely confounded by age and frailty. Furthermore, congestive heart failure was the only specified cardiovascular disease reported in one study, whereas the remaining studies used broad groupings. Identifying specific cardiovascular or cerebrovascular diseases associated with severe RSV infection was therefore not possible.

Overall, the evidence suggests a possible association between cardiovascular and cerebrovascular diseases and severe outcomes of RSV infection; however, the findings are not consistent enough to support solid conclusions.

Neurological disease

Neurological disease was evaluated in three low RoB studies and showed moderate effect estimates. Findings for hospitalisation were not consistent as one study found a moderate association after adjusting for unknown confounders, whereas another did not. A third study showed moderate association between dementia and all-cause death in adults aged ≥ 60 years after adjustment for potential confounding factors such as sex, prior hospitalisation, and other comorbidities.

Overall, the evidence suggests that neurological disease is a potentially relevant risk factor, especially in older adults; however, the findings are not fully consistent and do not allow firm conclusions.

Cancer and haematological malignancies

Cancer and haematological malignancies were evaluated in a limited number of studies and were primarily associated with mortality outcomes. Some studies, including at least one low RoB study, reported strong to very strong adjusted effect estimates. However, the evidence base was small, and findings may partly reflect underlying frailty, disease severity, or competing risks rather than RSV-specific effects.

Overall, the evidence suggests that cancer and haematological malignancies may be relevant risk factors for severe RSV outcomes, but the limited number of studies and potential confounding preclude firm conclusions.

Lifestyle

Smoking

Smoking was evaluated in only two studies. The adjusted analysis from the low RoB study showed a moderate effect, while the medium RoB study reported a strong crude effect, suggesting an increased risk of hospitalisation. No consistent association was found for mortality. Given the very limited adjusted data, it remains unclear whether the findings are independent of age or other underlying conditions.

Overall, the evidence suggests a possible association between smoking and hospitalisation, however, the evidence is very limited due to the small number of studies. Given that smoking is the leading cause of COPD in high-income countries, evaluating the relationship between smoking, COPD, and severe RSV infection outcomes would have been of clear interest. However, this was not reported in any of the included studies.

Remaining potential risk factors

Among other potentially relevant factors, the most robust evidence from low RoB studies did not support an association between sex as an independent risk factor for severe RSV outcomes. Evidence for other comorbidities, including kidney disease, liver disease, diabetes and immunosuppression, as well as lifestyle factors was limited in terms of the number and quality of available studies and the consistency of findings. Reported associations were typically weak, based on crude estimates, and frequently attenuated after adjustment for age or other confounders. Obesity was assessed in only one study, and no clear association was identified.

Comparison with previous reviews

These findings are broadly consistent with previous systematic reviews and meta-analyses of RSV in older adults, which have identified older age and chronic lung disease, particularly COPD, as possible risk factors of severe disease and hospitalisation. For example, Penders et al. 2025 [19] reported that adults with COPD (or asthma) were at increased risk of severe RSV infection outcomes, and Njue et al. 2023 [20] found that the risk of RSV-related hospitalisation in adults increased with age, particularly ≥ 65 years.

Previous reviews have also highlighted the potential role of comorbid conditions more broadly. Ivey et al. 2018 [21] concluded that older patients and those with underlying cardiac disease may be at increased risk of illness and morbidity due to RSV infection. However, in line with the findings of the present review, the evidence for cardiovascular disease remains uncertain, with many estimates based on unadjusted analyses and therefore susceptible to confounding by age and underlying frailty, as well as limited precision due to small sample sizes in some studies.

Furthermore, Njue et al. 2023 [20] reported that comorbid conditions (including cardiac, pulmonary, and immunocompromising diseases, diabetes, and kidney disease) were associated with increased hospitalisation risk in people aged < 65 years. This was not possible to evaluate in the current review, as most included studies focused on older, hospitalised populations. The review by Njue et al. differed in scope and eligibility criteria, including broader outcome definitions (e.g. lower respiratory tract infection, length of stay, and administrative ICD-10 coded diagnoses), and a wider range of comparator groups, whereas the present review focused on predefined clinical outcome transitions (e.g. outpatient to hospitalisation, hospitalisation to ICU admission or death) and excluded studies based solely on administrative ICD-10 coding.

A recent large matched cohort study done by Hviid et al. 2025 [22] found an increased long-term risk of cardiovascular events following RSV infection, particularly among older adults and those with pre-existing cardiovascular disease or diabetes. The largest risk was observed in older people aged ≥ 85 years and in adults aged ≥ 45 years with pre-existing cardiovascular disease or diabetes. While this supports the relevance of age and comorbidity in RSV-associated outcomes, it reflects longer-term complications rather than acute disease severity and is therefore not directly comparable to the outcomes assessed in this review.

Like earlier reviews, we found limited and inconsistent evidence for some clinical factors, likely reflecting underpowered and heterogenous studies. Njue et al. 2023 [20] observed similar inconsistencies and explained it as heterogeneity among study populations, risk factor definitions, adjustment for cofounders among the studies, limitations that also restrict generalisability in the current rapid review. Interestingly, other earlier reviews identified diabetes, obesity, kidney disease, neurologic diseases, and immunocompromised conditions as significant risk factors [20,23,24]. The weaker and less consistent evidence for these factors in the present review is likely due to the smaller number of included studies and their smaller cohort sizes.

Limitations of the evidence base

Several limitations in the evidence base (included studies) that hindered solid conclusions were identified. First, sample sizes were often small, resulting in statistically underpowered results—particularly for ICU admission and mortality outcomes—leading to imprecise estimates. Several clinical risk factors associated with severe outcomes lacked sufficient statistical power to support definitive conclusions.

Second, heterogeneity in study designs, risk factor definitions, and outcome definitions (e.g. differing thresholds for 'severe disease') hindered direct comparability between studies. In particular, risk factors were often defined broadly or inconsistently (e.g. grouped comorbidities or varying definitions of immunosuppression), limiting the ability to assess specific conditions and compare findings across studies. With the exception of age, most studies assessed risk factors as binary variables, limiting the ability to examine gradients of risk or associations across levels of the risk factor (e.g. varying degrees of disease or differences in biomarker levels). Many studies lacked multivariable adjustment for confounding factors, limiting confidence in causal inference.

Third, even though lab-confirmed RSV infection was an inclusion criterion, sensitivity and specificity variation among the methods used (e.g. use of antigen testing, PCR, or cell culture) may have introduced misclassification, including false negatives and incomplete case ascertainment.

Fourth, most evidence was derived from hospitalised or elderly cohorts, introducing selection bias and restricting generalisability to the wider adult population. Cohort studies investigating clinical risk factors in adults younger than 60 years old were extremely limited in this review, and no firm conclusions can be drawn for this age group. Larger, long-term, and possibly case-control cohort studies, particularly those including adults under 60 years old and conducted in community settings, are needed to clarify and validate potential clinical risk factors. Such studies would help improve understanding of at-risk adult populations and guide the targeting of preventive interventions, including vaccination.

Limitations of the rapid systematic review approach

This rapid systematic review has several limitations. Although a structured and predefined approach was used, including explicit inclusion criteria and transparent search strategies, the time-constrained methodology and scoped search restrictions may have resulted in some relevant studies being missed. In particular, studies using alternative terminology or not indexed within the selected databases may not have been captured. The exclusion of grey literature and non-peer-reviewed sources may also have limited the comprehensiveness of the evidence base.

Compared with a full systematic review, the rapid approach allows less opportunity for exhaustive searching, which may increase uncertainty in the findings. However, the restrictions were predefined and applied to ensure relevance and feasibility within the review timeframe.

Effect estimate thresholds were applied to facilitate structured comparison and synthesis across studies with heterogeneous designs and populations. This categorisation was intended as a descriptive framework to support consistency in interpretation. Small increases in risk may still be clinically important in high-risk populations, while large effect estimates may be uncertain if derived from limited or lower-quality evidence. Accordingly, effect magnitude was interpreted alongside confidence intervals, study-level risk of bias, and overall consistency of findings.

5. Conclusion

In conclusion, despite small and underpowered cohorts and the inability to undertake a meta-analysis, the available evidence suggests older age is among the more consistently examined risk factors, although findings are not uniform across studies and are often based on unadjusted or imprecise estimates with limited adjustment for key confounders, particularly age in comorbidity analyses. Among comorbidities, chronic lung disease, particularly COPD, shows some of the most consistent evidence of association with severe RSV outcomes; however, this is similarly limited by small study sizes, reliance on crude estimates, and inconsistent adjustment for age and other confounding factors. Evidence for other comorbidities is generally limited and uncertain: neurological disease and cancer or haematological malignancies show suggestive but inconsistent associations with important concerns regarding imprecision and confounding, whereas cardiovascular disease shows similarly inconsistent and methodologically limited evidence without clear differences in strength or consistency compared with other comorbidities. Most of the available studies evaluated these effects in older adult cohorts. Overall, these findings may help inform prioritisation of higher-risk groups for RSV vaccination, while acknowledging substantial uncertainty in the magnitude and independence of most associations.

Evidence gaps and future research priorities

Evidence for clinical risk factors in adults under 60 years is very limited, and it is unclear whether risk factors identified in older populations apply to this age group or to the same extent.

Few studies have compared outcomes in community-managed versus hospitalised patients, with most focusing on in-hospital progression, such as ICU admission or death. While understanding factors linked to in-hospital deterioration and mortality is critical, identifying those that predict progression from community care to hospitalisation is equally important for prioritising high-risk groups for preventive interventions.

Evidence on risk associated with immunosuppression is also limited, with few studies reporting outcomes specifically by type or degree of immunosuppression, making it difficult to differentiate their impact on disease severity.

Additionally, few studies have explored interactions between risk factors (e.g. age and comorbidity) or quantified the contribution of multimorbidity to severe outcomes. Understanding these interactions could clarify whether multimorbidity adds compounded risk, enhancing risk stratification and informing targeted preventive strategies.

Future research should prioritise large, sufficiently powered, prospective cohort and case-control studies. Greater inclusion of younger adults (<60 years), immunocompromised individuals, and people with diverse comorbidity profiles would strengthen risk stratification and better inform targeting of preventive strategies for severe RSV disease. Furthermore, inclusion of longer-term outcomes (e.g. 1–5 year morbidity and mortality) would support better characterisation of both the immediate and sustained impact of RSV infection.

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Annex 1. Search strategy

Final searches for peer-reviewed literature were conducted on 2 September 2025. The search strings and number of results are shown below.

PubMed search:

	Population	# Hits
Search #	Search string: RSV	
1	"Respiratory Syncytial Virus Infections" [Mesh]	10360
2	"Respiratory Syncytial Viruses" [Mesh]	11916
3	RSV [tiab]	18331
4	"Respiratory Syncytial Virus*" [tiab]	19692
5	"Respiratory Syncytial virus infection*" [tiab]	2939
6	"RS virus*" [tiab]	449
7	#1 OR #2 OR #3 OR #4 OR #5 OR #6	27419
	Search string: Adults	
8	"Adult" [Mesh]	8512426
9	"Aging" [Mesh]	311888
10	"Aged" [Mesh]	3741913
11	Adult* [tiab]	1794972
12	Ageing [tiab]	64761
13	Aged [tiab]	859970
14	Elderly [tiab]	326521
15	Senior [tiab]	48963
16	#8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15	9919692
	Search string: RSV + Adults	
17	#7 AND #16	6554
	Intervention	

	Population	# Hits
	Search string: Clinical risk factors	
18	"Risk Factors" [Mesh]	1050980
19	"Odds Ratio" [MeSH]	99055
20	Risk* [tiab]	3442222
21	"Risk factor*" [tiab]	901812
22	Predictor* [tiab]	582809
23	Association* [tiab]	1996316
24	Impact [tiab]	1733025
25	Determinant* [tiab]	327644
26	"odds ratio*" [tiab]	431704
27	"hazard ratio*" [tiab]	205786
28	"risk ratio*" [tiab]	44817
29	#18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28	6882094
	Outcomes	
	Search string: Hospitalisation/ICU/Death	
30	Hospitalization [Mesh]	319984
31	"Intensive Care Units"[Mesh]	118421
32	Death [Mesh]	172367
33	Mortality [Mesh]	444239
34	Hospitalization* [tiab]	233199
35	Hospitalisation*	30355
36	"Intensive Care Unit*" [tiab]	183250
37	Death [tiab]	996933
38	Mortalit* [tiab]	1155935
39	Fatal* [tiab]	201941

	Population	# Hits
40	#30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39	2864580
	Geographical regions	
	Search string: Europe (EU/EEA)	
41	Austria [tiab]	17240
42	Belgium [tiab]	21771
43	Bulgaria [tiab]	5732
44	Croatia [tiab]	8473
45	Cyprus [tiab]	3067
46	Czech* [tiab]	21385
47	Denmark [tiab]	38458
48	Estonia [tiab]	3491
49	Finland [tiab]	32057
50	France [tiab]	83877
51	Germany [tiab]	113898
52	Greece [tiab]	20921
53	Hungary [tiab]	13826
54	Iceland [tiab]	6216
55	Ireland [tiab]	29819
56	Italy [tiab]	95088
57	Latvia [tiab]	2107
58	Lietchenstein [tiab]	477
59	Lithuania [tiab]	4114
60	Luxembourg [tiab]	1529
61	Malta [tiab]	1863
62	Netherlands [tiab]	65237

	Population	# Hits
63	Norway [tiab]	40564
64	Poland [tiab]	35664
65	Portugal [tiab]	18711
66	Romania [tiab]	9682
67	Slovakia [tiab]	4968
68	Slovenia [tiab]	4993
69	Spain [tiab]	81506
70	Sweden [tiab]	62075
	Search string: Europe (non-EU/EEA)	
71	Europe [Mesh]	1631133
72	Europe* [tiab]	418405
73	Switzerland [tiab]	33705
74	"United Kingdom" [tiab]	56863
75	England [tiab]	70060
76	Scotland [tiab]	20929
77	Wales [tiab]	30735
78	"Northern Ireland" [tiab]	6396
	Search string: Other comparable health care settings	
79	"North America"[Mesh]	1764303
80	America [tiab]	135564
81	"United States" [tiab]	368364
82	US [tiab]	762875
83	USA [tiab]	135529
84	Canada [tiab]	127018
85	Australia [tiab]	137090

	Population	# Hits
86	"New Zealand" [tiab]	70160
87	Japan [tiab]	167064
88	"South Korea" [tiab]	24416
89	#41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54 OR #55 OR #56 OR #57 OR #58 OR #59 OR #60 OR #61 OR #62 OR #63 OR #64 OR #65 OR #66 OR #67 OR #68 OR #69 OR #70 OR #71 OR #72 OR #73 OR #74 OR #75 OR #76 OR #77 OR #78 OR #79 OR #80 OR #81 OR #82 OR #83 OR #84 OR #85 OR #86 OR #87 OR #88	5046409
	Combined	
	RSV AND Risk factors AND Outcomes AND Geographical areas	
90	#17 AND #29 AND #40 AND #89	603

Embase search:

	Population	# Hits
Search #	Search string: RSV	
1	exp Respiratory Syncytial Virus Infection/	11359
2	RSV.ti,ab	24857
3	respiratory syncytial virus'.ti,ab.	24227
4	Respiratory Syncytial Virus Infection*':ti,ab	3430
5	RS virus*'.ti,ab.	510
6	#1 OR #2 OR #3 OR #4 OR #5 OR #6	35756
	Search string: Adults	
7	exp adult/	12661390
8	exp aging/	366513
9	exp aged/	4326641
10	adult*.ti,ab	2446130
11	aging*.ti,ab	340006

	Population	# Hits
12	aged.ti,ab	1185383
13	elderly.ti,ab	458584
14	senior.ti,ab	70482
15	#7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14	14079764
	Search string: RSV + Adults	
16	#6 AND #15	10502
	Intervention	
	Search string: Clinical risk factors	
17	exp risk factor/	1603907
18	exp odds ratio/	36644
19	risk*.ti,ab	5003682
20	predictor*.ti,ab	875665
21	association*.ti,ab	2919342
22	impact*.ti,ab	2817222
23	determinant*.ti,ab	393977
24	odds ratio*.ti,ab	544756
25	hazard ratio*.ti,ab	294266
26	risk ratio*.ti,ab	57743
27	#17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 #24 OR #25 OR #26	10021359
	Outcomes	
	Search string: Hospitalisation/ICU/Death	
28	exp hospitalization/	666413
29	exp intensive care unit/	378434
30	exp death/	2289829
31	exp mortality/	1589292

	Population	# Hits
32	Hospitalization*.ti,ab.	410431
33	Hospitalisation*.ti,ab	49890
34	Intensive Care Unit*'.ti,ab	268037
35	Death [tiab]	1438737
36	Mortality* [tiab]	1729390
37	Fatal* [tiab]	272697
38	#28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37	4510276
	Combined	
	RSV AND Risk factors AND Outcomes	
39	#16 AND #27 AND #38	2575
	Geographical regions	
	Search string: Europe (EU/EEA)	
40	Austria.ti,ab	25690
41	Belgium.ti,ab	32102
42	Bulgaria.ti,ab	8410
43	Croatia.ti,ab	12526
44	Cyprus.ti,ab	3993
45	Czech*.ti,ab	704
46	Denmark.ti,ab	51306
47	Estonia.ti,ab	4850
48	Finland.ti,ab	38688
49	France.ti,ab	129406
50	Germany.ti,ab	174096
51	Greece.ti,ab	28198
52	Hungary.ti,ab	20575

	Population	# Hits
53	Iceland.ti,ab	7267
54	Ireland.ti,ab	176122
55	Italy.ti,ab	128119
56	Latvia.ti,ab	3121
57	Liechtenstein.ti,ab	566
58	Lithuania.ti,ab	5267
59	Luxembourg.ti,ab	1987
60	Malta.ti,ab	2547
61	Netherlands.ti,ab	91693
62	Norway.ti,ab	49483
63	Poland.ti,ab	45261
64	Portugal.ti,ab	26255
65	Romania.ti,ab	14045
66	Slovakia.ti,ab	6740
67	Slovenia.ti,ab	7244
68	Spain.ti,ab	109988
69	Sweden.ti,ab	80514
70	Search #40 to #70 combined with OR	1070873
	Search string: Europe (non-EU/EEA)	
71	exp Europe/	1936635
72	Europe*.ti,ab	908270
73	Switzerland.ti,ab	61338
74	United Kingdom'.ti,ab	71887
75	England.ti,ab	92693
76	Scotland.ti,ab	27561

	Population	# Hits
77	Wales.ti,ab	39300
78	Northern Ireland'.ti,ab	8823
79	#71 - #78 combined with OR	2624354
80	#70 (EU/EEA) OR #79 (EU/EEA and other European countries)	2990363
	Search string: North America	
81	exp United States/	1465217
82	America.ti,ab	197237
83	United States'.ti,ab	454920
84	US.ti,ab	923936
85	USA.ti,ab	269865
86	Canada.ti,ab	165583
87	#81 - #86 combined with OR	2864542
	Search string: Australia / New Zealand	
88	Australia.ti,ab	174200
89	New Zealand.ti,ab	89671
90	#88 OR #89	245687
	Search string: Japan/ South Korea	
91	Japan.ti,ab	256706
92	South Korea'.ti,ab	28771
93	#91 OR #92	282504
	Combined	
	RSV AND Risk factors AND Outcomes AND Geographical areas	
	#39 AND (#80 OR #87 OR #90 OR #93)	954

Cochrane Library search:

	Population	# Hits
Search #	Search string: RSV	
1	MeSH descriptor: [Respiratory Syncytial Virus Infections] explode all trees	587
2	MeSH descriptor: [Respiratory Syncytial Viruses] explode all trees	319
3	Respiratory NEXT Syncytial NEXT Virus*:ti,ab	1200
4	Respiratory NEXT Syncytial NEXT virus NEXT infection*:ti,ab	200
5	RSV:ti,ab	1336
6	RS NEXT virus:ti,ab	13
7	#1 OR #2 OR#3 OR #4 OR #5 OR #6	1663
	Search string: Adults	
8	MeSH descriptor: [Adult] explode all trees	631544
9	MeSH descriptor: [Aged] explode all trees	283838
10	Adult*:ti,ab	234263
11	Ageing:ti,ab	13948
12	Aged:ti,ab	185064
13	Elderly:ti,ab	57256
14	Senior:ti,ab	4555
15	#8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14	924666
	Search string: RSV + Adults	
16	#7 AND #15	760
	Intervention	
	Search string: Clinical risk factors	
17	MeSH descriptor: [Risk factors] explode all trees	38124
18	MeSH descriptor: [Odds Ratio] explode all trees	4430
19	Risk*:ti,ab	304457

20	Risk NEXT Factor*:ti,ab	56887
21	Predictor*:ti,ab	40526
22	Association*:ti,ab	94902
23	Impact:ti,ab	173623
24	Determinant*:ti,ab	10818
25	"odds ratio*":ti,ab	29437
26	"hazard ratio*":ti,ab	33576
27	"risk ratio*":ti,ab	8418
28	#17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27	550736
	Outcomes	
	Search string: Hospitalisation/ICU/Death	
29	MeSH descriptor: [Hospitals] explode all trees	5749
30	MeSH descriptor: [Intensive Care Units] explode all trees	6385
31	MeSH descriptor: [Death] explode all trees	3508
32	MeSH descriptor: [Mortality] explode all trees	18585
34	Hospitalisation*:ti,ab	6633
35	Intensive NEXT Care NEXT Unit*:ti,ab	23379
36	Death:ti,ab	92346
37	Mortalit*:ti,ab	133167
38	Fatal*:ti,ab	13756
39	#29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38	246672
	Combined	
	RSV AND Risk factors AND Outcomes	
40	#16 AND 28 AND 39	105
	Geographical regions	
	Search string: Europe (EU/EEA)	

41	Austria:ti,ab	2178
42	Belgium:ti,ab	2532
43	Bulgaria:ti,ab	228
44	Croatia:ti,ab	216
45	Cyprus:ti,ab	138
46	Czech*:ti,ab	1017
47	Denmark:ti,ab	5050
48	Estonia:ti,ab	173
49	Finland:ti,ab	2279
50	France:ti,ab	7319
51	Germany:ti,ab	12790
52	Greece:ti,ab	1069
53	Hungary:ti,ab	711
54	Iceland:ti,ab	245
55	Ireland:ti,ab	2495
56	Italy:ti,ab	6240
57	Latvia:ti,ab	86
58	Lietchenstein:ti,ab	0
59	Lithuania:ti,ab	161
60	Luxembourg:ti,ab	65
61	Malta:ti,ab	55
62	Netherlands:ti,ab	9084
63	Norway:ti,ab	2939
64	Poland:ti,ab	1460
65	Portugal:ti,ab	888
66	Romania:ti,ab	396

67	Slovakia:ti,ab	123
68	Slovenia:ti,ab	247
69	Spain:ti,ab	6092
70	Sweden:ti,ab	6534
71	Search #41 - #70 combined with OR	60728
	Search string: Europe (non-EU/EEA)	
72	MeSH descriptor: [Europe] explode all trees	43241
73	Europe*:ti,ab	40816
74	Switzerland:ti,ab	4579
75	United NEXT Kingdom:ti,ab	4646
76	England:ti,ab	4923
77	Scotland:ti,ab	1563
78	Wales:ti,ab	2041
79	Northern NEXT Ireland:ti,ab	518
80	#72 OR #73 OR #74 OR #75 OR #76 OR #77 OR #78 OR #79	92786
81	#71 (EU/EEA) OR #80 (EU/EEA and other European countries)	131665
	Search string: North America	
82	MeSH descriptor: [North America] explode all trees	34754
83	America:ti,ab	6152
84	United NEXT States:ti,ab	19973
85	US:ti,ab	46800
86	USA:ti,ab	21068
87	Canada:ti,ab	10878
88	#82 OR #83 OR #84 OR #85 OR #86 OR #87	120754
	Search string: Australia / New Zealand	
89	Australia:ti,ab	13482

90	New NEXT Zealand:ti,ab	7949
91	#89 OR #90	18130
	Search string: Japan/South Korea	
92	Japan:ti,ab	12883
93	South NEXT Korea:ti,ab	1595
94	#92 OR #93	14251
	Combined	
	RSV AND Risk factors AND Outcomes AND Geographical areas	
95	#40 AND (#81 OR #88 OR #91 OR #94)	37

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