

# Cardiovascular Complications Following Respiratory Syncytial Virus Infection: A Systematic Review

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## Abstract

### Background

Respiratory Syncytial Virus (RSV) is widely recognized as a respiratory pathogen, but emerging evidence suggests it also leads to significant cardiovascular complications. The objective of this systematic review was to identify and summarize evidence on cardiovascular complications associated with RSV infection, specifically the types, prevalence and risks of cardiovascular events linked to RSV

### Methods

A systematic search of PubMed, Embase, and Web of Science databases was conducted using the keywords “respiratory syncytial virus” and “cardiac complication.” Observational studies reporting laboratory-confirmed RSV infection and associated cardiovascular complications, and published in English were included. Articles were screened using Covidence software. Cardiovascular adverse events, prevalence and risks were narratively summarized.

### Results

Of 287 records identified, nine studies comprising seven primary observational studies and two review articles comprising adult and/or pediatric populations, were included. Cardiovascular complications commonly reported included myocardial infarction, heart failure, and arrhythmias, particularly in hospitalized adults aged over 65 years. The prevalence of cardiovascular complications ranged 8% to 24.6% in hospitalized patients; 51% of high-risk hospitalized adults developed cardiac complications. Adults with pre-existing cardiovascular conditions were at greater risk (adjusted risk ratio 3.51 [95% confidence interval, CI 2.38 – 5.89]. Adults with pre-existing coronary arterial disease also had an increased odds of cardiovascular complications (adjusted OR 6.18, 95% CI 1.18–32.5). Cardiovascular complications were less frequently reported among children.

### Conclusions

This review suggests a significant burden of cardiovascular complications following RSV infection, notably among older adults. High-risk groups could benefit from targeted preventive measures such as RSV vaccination programs.

**Keywords:** Respiratory Syncytial Virus, Cardiovascular Complications, Systematic Review

## Introduction

Respiratory syncytial virus is a significant global public health concern that causes nearly 33 million cases of lower respiratory tract infections (LRTIs) annually and leads to 3.6 million hospitalizations and more than 100,000 deaths in children aged less than 5 years.<sup>1</sup> In the United States, RSV causes an estimated 58,000–80,000 hospitalizations and 100–300 deaths annually in children aged less than five years.<sup>2</sup> In Taiwan, the incidence of RSV infection was 232 per 100,000 children-years in children aged less than 5 years.<sup>3</sup> Adults also carry a significant burden of RSV in the United States, with the virus being responsible for 160,000 hospitalizations of adults each year, and 10,000 deaths among adults over 65 years.<sup>4</sup> The hospitalization costs range from \$8,700 to \$9,690 per patient over 10 years, with costs being higher for patients with significant heart disease or infants born at 36 weeks' gestation.<sup>5</sup> This significant global burden of RSV highlights the importance of identifying populations at the highest risk of infection and severe outcomes.

People at the highest risk of acquiring RSV include premature babies, infants less than 6 months of age, children with weakened immune systems, children with neuromuscular disorders, active tobacco smokers, patients with a pre-existing cardiac disease, adults aged 65 years or older, and adults with

underlying medical conditions such as asthma, chronic obstructive pulmonary disease, or congestive heart failure.<sup>1,6-8</sup> In urban settings, particularly among immigrant communities, factors such as overcrowded living conditions, limited access to healthcare, and language or cultural barriers can further elevate the risks associated with RSV infection. Indeed, refugees and asylum seekers experience a higher burden of RSV infection, with a pooled prevalence estimate of approximately 13%, showing increased vulnerability among immigrant populations.<sup>9</sup> Additionally, it is estimated that by 2050, around 68% of the global population will reside in urban areas, increasing the potential public health impact of infectious diseases like RSV.<sup>10</sup>

RSV outbreaks occur in a seasonal pattern in most parts of the world.<sup>11</sup> This pattern is influenced by geographical factors like latitude and altitude, and meteorological factors like temperature and relative humidity.<sup>11-12</sup> In temperate regions, RSV outbreaks typically last for 2 to 5 months, with peak incidence being during winter months, when there are low temperatures and high relative humidity.<sup>13</sup> In tropical regions, outbreaks have longer durations with the peak aligning with the rainy season.<sup>14</sup> In regions near the equator that receive high yearly rainfall, RSV activity persists throughout the year or for large portions of the year.<sup>15-16</sup>

RSV infection is not only a leading cause of respiratory illness but is also associated with cardiovascular complications like myocarditis, atherosclerosis, congestive heart failure (CHF), acute coronary syndrome, and arrhythmias. Cardiovascular complications are reported to occur in 45-63% of all RSV-related hospitalizations and 14-22% of adult RSV cases.<sup>3,4</sup> A study in China found an association between RSV and myocardial infarction (adjusted odds ratio, OR: 11.1 (95% confidence interval, CI: 3.3-29.5).<sup>18</sup> Like other viral and bacterial infections, RSV infection has been suggested to contribute to the increased risk of myocardial infarction through prolonged or recurrent inflammation and plaque destabilization.<sup>3</sup> The release of pro-inflammatory cytokines such as interleukin-6 (IL-6), IL-1 $\beta$ , and tumor necrosis factor-alpha causes this inflammatory response, which can adversely affect cardiovascular function.<sup>22</sup> Evidence suggests that RSV can also cause direct myocardial injury.<sup>33</sup> IL-6 and IL-8 levels were significantly higher than 200 times the upper limit of normal in a case report of two young, healthy children who died suddenly from cardiac collapse with acute RSV bronchiolitis.<sup>22</sup> Cardiovascular RSV complications may also contribute to higher mortality in hospitalized patients. In another study, acute cardiovascular events were found to cause immediate death in 16.7% of the 72 patients who died within 60 days of hospitalization; cardiovascular complications were associated with a higher risk of death (adjusted hazard ratio, HR: 1.71 (95% CI).<sup>19</sup>

There is a lack of literature summarizing the spectrum and burden of cardiovascular complications following RSV infection, which could inform public health planning and effective preventive measures to reduce RSV-associated morbidity and mortality, particularly the high-risk groups, including vulnerable groups such as urban residents and immigrant populations. So, the research questions for this literature review were: among individuals with RSV diagnosis, what are the cardiovascular complications following RSV infection, and what are the prevalence, and risks of cardiovascular complications? The objectives of this systematic literature review were to identify and summarize evidence regarding the cardiovascular complications associated with RSV infection, focusing on types, prevalence, and risks of cardiovascular events linked to RSV.

## Methods

I performed a systematic review to identify studies that reported cardiovascular complications associated with RSV infection to determine the prevalence and incidence of RSV-associated cardiac complications.

### Search Strategy and Eligibility Criteria

I searched PubMed, Embase, and Web of Science databases using the keywords “respiratory syncytial virus” AND “cardiac

complication” on 22 February 2025. The search was limited to human studies, used an observational design, including cross-sectional, cohort or case-control study design, review, or systematic review, and published in English. One additional article was found by hand-searching relevant references. All identified records were imported into online reference management software Covidence<sup>20</sup>, which helped with removing duplicates and screening.

### Study Selection

After duplicates were removed manually and automatically by Covidence, first titles and abstracts were screened, then full-text screening was done to finalize studies for inclusion. Studies were included if they reported RSV infection and provided data on at least one cardiovascular complication (e.g., myocardial infarction, heart failure, arrhythmias, or stroke) associated with RSV infection. Articles unrelated to RSV or lacking RSV-associated cardiovascular outcome data were excluded. I excluded case reports, case series, editorials, commentaries, or conference abstracts without sufficient data on cardiovascular outcomes, and general review articles on RSV.

### Data Extraction

For the included studies, I used an Excel file to extract study characteristics (e.g., authors, publication year, country, study design, sample size), characteristics of the sample (e.g., age and sex distribution, pre-existing comorbidities, setting), method of RSV confirmation (e.g., RT-PCR), key findings of prevalence or incidence of cardiac events, odds ratios, or relative risks, and limitations of the study.

### Data Synthesis

The characteristics of the included studies are summarized and presented in a table. The prevalence of different cardiac complications, odds ratios and relative risks were narratively reported along with study limitations in a separate table.

## Results

The initial search yielded a total of 287 studies. After removing duplicates, 262 records remained for title and abstract screening. During this stage, 139 studies were excluded for either lacking an RSV focus or providing no cardiac outcome data. The full-text screening was performed for 123 articles, of which six could not be retrieved and 107 did not meet the inclusion criteria (Figure 1). 10 articles meeting all inclusion criteria were included for data extraction. One article was further excluded for having duplicate results included in a review article. This resulted in a total of nine articles included in the review. This resulted in a total of nine articles included in the review.<sup>21-29</sup>

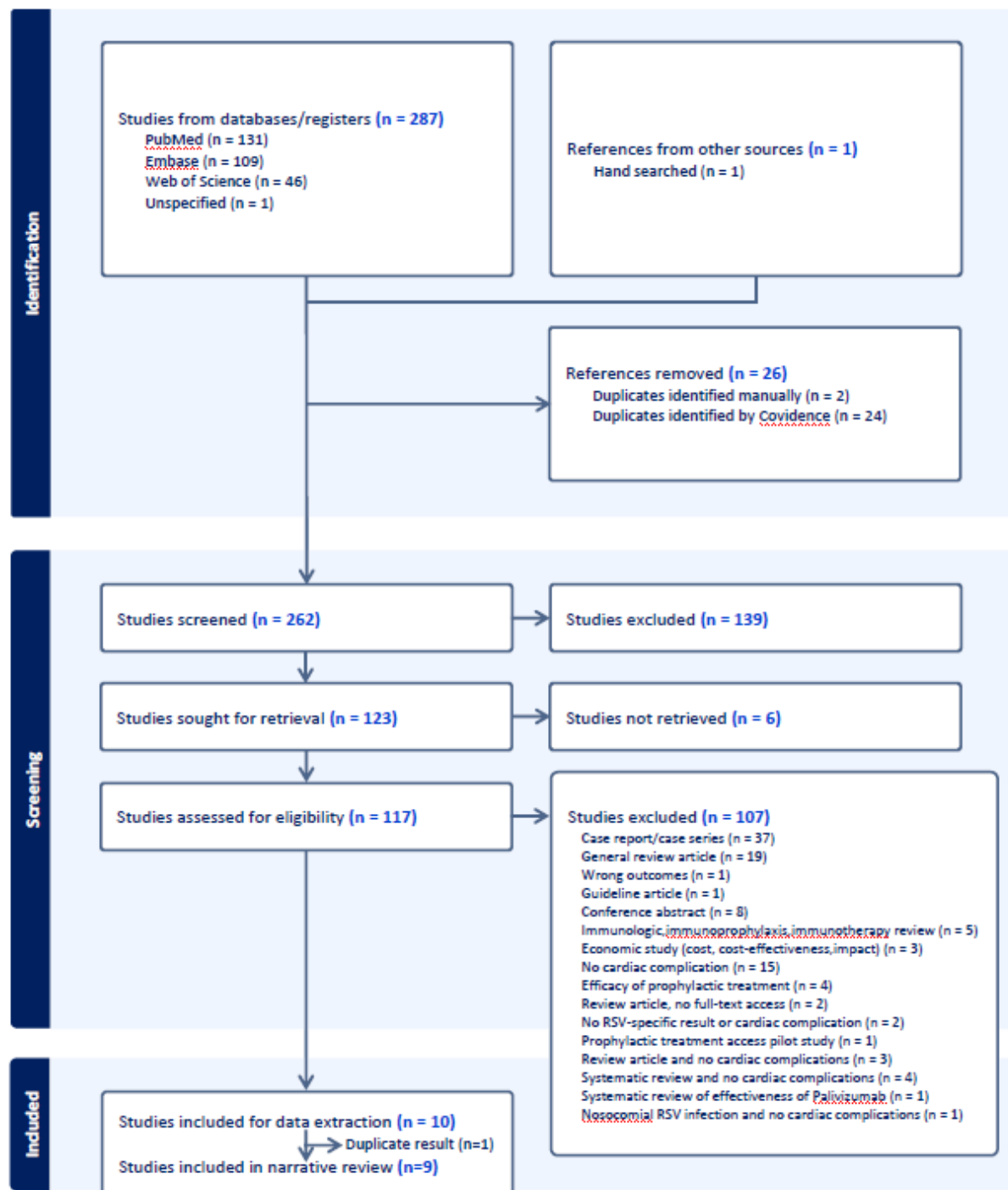


Figure 1. PRISMA Flow Diagram of included studies

### Characteristics of Included Studies

Of the nine articles included in this review, two were review articles<sup>21-22</sup> and seven were primary research articles<sup>23-29</sup> of different designs, including cross-sectional, case-control and cohort (Table 1). Most of the primary studies were conducted in high-income country setting; only one study was from upper-middle income country Thailand. The nine included articles covered both adult and pediatric populations, mostly hospitalized patients. The studies used molecular testing (e.g., RT-PCR) to laboratory-confirm RSV infection, and ICD-9 and ICD-10 diagnostic codes to identify RSV infections in health administrative data. Sample sizes ranged from fewer than 100 participants to several thousand. Most of the studies focused on hospitalized patients with RSV.

### Cardiovascular Outcomes Following RSV Infection

Most of the studies reported multiple cardiovascular complications, with acute myocardial infarction, congestive heart failure, and

arrhythmias being the most common (Table 2). Congestive heart failure included both worsening or exacerbation and new onset. Other cardiac complications included different types of tachycardia (e.g., atrial, supraventricular), cardiogenic shock, heart block, sudden cardiac arrest, myocarditis, pericarditis, endocarditis, cardiomyopathy, and Kawasaki disease.

The mean or median age of the adults with RSV infection were older than 70 years, and the majority of the adult patients were females (Table 1). Between 26% and 100% adult patients with RSV infection had at least one comorbidity.

Across studies, the reported prevalence of any cardiac complication ranged from approximately 8% to 24.6% in hospitalized patients overall. Up to about half (51%) of the high-risk hospitalized adults developed cardiac complications like arrhythmias and myocardial infarction. Heart failure and arrhythmias were prevalent, particularly in older adults aged  $\geq 65$  years or those with pre-existing comorbidities. Arrhythmias and

myocardial infarction were also reported in non-hospitalized outpatients with and without high-risk.<sup>29</sup> The adjusted risk ratio of acute cardiac event of any category, acute heart failure and acute ischemic heart disease in hospitalized adults were 2.38 – 5.89 times higher in patients with pre-existing cardiovascular disease compared to patients without any pre-existing cardiovascular disease<sup>28</sup>. Another study reported an increased odds of overall cardiovascular complications in hospitalized adult patients with RSV infection who had pre-existing coronary arterial disease (adjusted odds ratio, OR 6.18, 95% CI 1.18–32.5).<sup>23</sup>

In the three primary studies on children, the prevalence of cardiovascular complications following RSV was low.<sup>25-27</sup> One

study found cardiovascular complications in 1.5% (1,575 out of 103,185) hospitalized children.<sup>6</sup> Another study found cardiac complications in 14% (13 out of 112) episodes of RSV infection in hospitalized children with pre-existing heart disease, and in 0.32% (10 out of 3201) episodes of RSV infection in hospitalized children without heart disease or other chronic conditions.<sup>26</sup> Yet another study found that 6% of the children with risk factors for severe RSV disease required mechanical ventilation due to cardiac complications, while 2% children without risk factors developed cardiac complications.<sup>27</sup>

**Table 1: Characteristics of the studies included in the review**

Author, year	Country	Study design	Study period	Study participants	Sample size and characteristics	Exposure
Chuaychoo et al., 2019 [23]	Thailand	Cohort (retrospective and prospective)	May 2014 - December 2015	Hospitalized patients aged $\geq 15$ years and diagnosed with RSV infection	RSV was detected in 86 of 1562 (5.5%) adult hospitalized patients suspected of respiratory viral infection. <b>69</b> patients were included in the study.  <b>Age, median (IQR):</b> 72 (IQR 58–81) years <b>Sex:</b> 52 (75.4%) females	RSV infection diagnosed by real-time reverse transcriptase polymerase chain reaction (RT-PCR) and/or indirect immunofluorescence assay (IFA)
Descamps et al., 2021 [24]	France	Observational using data from a prospective multicentre study	2017/2018 and 2018/2019 winter seasons (late October to mid-April)	Adults hospitalised for at least 24 hours for influenza-like illness (ILI) with symptom onset $<7$ days before swabbing at 5 French University hospitals	Among 1428 hospitalised adults with ILI, RSV was detected in 8% (114 of 1428), including 6 with co-infections. <b>108</b> hospitalised adults without co-infections were included.  <b>Age, mean (range):</b> 73 (30–97) years <b>Sex:</b> Not reported	Laboratory-confirmed RSV infection using multiplex RT-PCR
Díez-Domingo et al., 2014 [21]	Not applicable	Systematic review	Studies published between 1950 and 2012	Studies on RSV incidence, impact on health, impact on healthcare resources, impact on direct and indirect cost, and strategies to reduce the impact	89 articles were included in the review. <b>One primary study article and one systematic review</b> included were on cardiac complications of RSV.	RSV infection
Ivey et al., 2018 [22]	Not applicable	Review	Not reported	Included studies related to RSV infection and cardiovascular disease in adults	Included <b>6 articles</b> that reported prevalence of cardiovascular complications associated with RSV infection	RSV infection
Khanal et al., 2024 [25]	United States	Retrospective, Cross-sectional	2020-2021	Children and young adults ( $\leq 20$ years) hospitalized for COVID-19, RSV, and influenza in the National Inpatient Sample (NIS) data	Of 212,655 respiratory virus admissions, <b>103,185</b> were due to RSV.  <b>Age, median (IQR):</b> $<1$ (0-1) years <b>Sex:</b> 46,445 (45.0%) females	RSV infection identified using ICD-10-CM codes B97.4, J12.1, J20.5, and J21.0

Lee et al., 2019 [26]	Hong Kong	Case control	2013-2015	RSV infection in children hospitalized in four local regional hospitals	3538 RSV hospitalisations occurred (entire cohort). Of these <b>112 episodes</b> were in <b>105 patients with heart disease (HD)</b> , 3201 episodes in <b>3155 patients with no heart disease (control)</b> , and <b>225</b> had chronic diseases other than heart disease or social problems.  RSV children were primarily aged <5 years <b>Age, median (IQR):</b> 0.9 (0.46-1.97) years in HD group and 1.19 (0.45-2.4) years in controls <b>Sex:</b> 56.3% of patients with HD and 56.9% of controls were male	RSV infection identified using ICD-9 codes 079.6 (0), 466.0 (9), 466.11, 480.1 and laboratory-confirmation by immunofluorescent antigen staining or RT-PCR
Nygaard et al., 2023 [27]	Denmark	Cohort (retrospective)	2016–17, 2017–18, 2018–19, 2019–20, and 2021–2022	Patients aged 0–17 years admitted to hospital with RSV	310423 children (aged 0–17 years) admitted to hospital with RSV. Of these, <b>133</b> received mechanical ventilation	Laboratory-confirmed RSV
Woodruff et al., 2024 [28]	United States	Cross-sectional	2014-2015 through 2017-2018 and 2022-2023	Hospitalized adults aged 50 years or older with RSV infection.	6248 <b>Age, median (IQR):</b> 72.7 (63.0 - 82.3) years <b>Sex:</b> 59.6% female and 40.4% male	Laboratory-confirmed RSV
Wyffels et al., 2020 [29]	United States	Cohort (retrospective)	2011-2015	Hospitalized or outpatient adults (at least 18 years of age) with at least 1 diagnostic code for RSV with continuous Medicare medical and pharmacy benefits	<b>1795</b> ; 793 hospitalized (756 high-risk) and 835 outpatients (399 high-risk). <b>Age, mean (SD):</b> <u>Hospitalized high-risk patients:</u> 77.1 (13.4) years <u>Hospitalized non-high-risk patients:</u> 71.9 (17.1) years <u>Outpatient high-risk patients:</u> 73.6 (14.5) years <u>Outpatient non-high-risk patients:</u> 71.1 (12.3) years  <b>Sex:</b> 563 male and 1065 female	RSV diagnosed using ICD-9-CM codes 079.6, 466.11, 480.01 and ICD-10-CM codes B97.4, J20.5, J12.1, J21.0

**Table 2: Cardiovascular complications associated with respiratory syncytial virus infection**

Author, year	Key findings	Limitations
Chuaychoo et al., 2019 [23]	<ul style="list-style-type: none"> <li>All 69 patients had at least one comorbidity</li> <li>17 of 69 patients (24.6%) developed cardiovascular complications:               <ul style="list-style-type: none"> <li>Worsening and new onset congestive heart failure (CHF) in 9 (13.0%)</li> <li>Acute myocardial infarction (MI) (non-ST-elevation MI {NSTEMI}) in 7 (10.1%)</li> <li>New atrial fibrillation in 4 (5.8%)</li> <li>Supraventricular tachycardia in 3 (4.3%)</li> </ul> </li> <li>9 of 17 (52.9%) patients had pre-existing cardiovascular diseases (CVD)</li> <li>Pre-existing coronary arterial disease (CAD) was associated with an increased odds of overall cardiovascular complications in hospitalized adult patients with RSV infection (OR 6.18, 95% CI 1.18–32.5, <math>p=0.03</math>) adjusted for age, sex, hypertension, dyslipidemia, diabetes mellitus, pre-existing CHF, arrhythmia, and VHD</li> <li>Acute MI accounted for 2 of 11 (18.2%) deaths</li> </ul>	Potential for selection bias as only the respiratory specimens of patients suspected of respiratory viral infection were sent for the detection of RSV
Descamps et al., 2021 [24]	<ul style="list-style-type: none"> <li>90% of the 108 RSV patients had at least one chronic condition, particularly chronic respiratory or cardiac diseases</li> <li>16 (15%) developed acute heart failure</li> </ul>	Despite the large patient group, the study has the potential to underestimate RSV cases due to its influenza-focused definition
Díez-Domingo et al., 2014 [21]	<ul style="list-style-type: none"> <li>Cardiovascular complications were found in 9% of infants under 12 months of age admitted for RSV-induced acute bronchiolitis and community-acquired pneumonia.</li> <li>Cardiovascular complications reported in this systematic review included:               <ul style="list-style-type: none"> <li>Atrial and supraventricular tachycardias</li> <li>Life-threatening arrhythmias</li> <li>Cardiogenic shock</li> </ul> </li> <li>Elevated cardiac troponin levels (indicating myocardial damage) found in 35% to 54% of infants with RSV infection ventilated in PICUs</li> </ul>	Not reported
Ivey et al., 2018 [22]	<ul style="list-style-type: none"> <li>Cardiovascular complications reported in up to 22% of RSV hospitalized cases:               <ul style="list-style-type: none"> <li>Acute heart failure in 19%</li> <li>Congestive heart failure exacerbation, atrial fibrillation, acute coronary event, or acute cerebrovascular event in 14.3% to 20.7%</li> <li>Congestive heart failure exacerbation in 14%</li> <li>New arrhythmia in 8%</li> <li>Myocardial infarction in 1%</li> <li>Congestive heart failure in 13–20% cases</li> </ul> </li> </ul>	Not reported
Khanal et al., 2024 [25]	<ul style="list-style-type: none"> <li>16,690 (26%) of 103,185 RSV hospitalized children had a comorbidity</li> <li>Cardiovascular complications included               <ul style="list-style-type: none"> <li>Myocarditis in 65 (0.1%)</li> <li>Tachyarrhythmia in 635 (0.6%)</li> <li>Supraventricular arrhythmia in 355 (0.34%)</li> <li>Ventricular arrhythmia in 180 (0.2%)</li> <li>Bradyarrhythmia/heart block in 205 (0.2%)</li> <li>Sudden cardiac arrest in 135 (0.1%)</li> </ul> </li> </ul>	Because of the use of the NIS medical and billing database of inpatient records, the findings may not be generalizable to outpatient settings or patients who were transferred between hospitals. The NIS may contain incorrect or missing information, resulting in potential inaccuracies.
Lee et al., 2019 [26]	<ul style="list-style-type: none"> <li>Cardiac complications were observed in hospitalized children with and without heart disease</li> <li>Cardiac complications in the heart disease group (112 episodes in 105 patients) included               <ul style="list-style-type: none"> <li>Heart failure exacerbation (n=13) and</li> <li>Arrhythmia (n=3)</li> </ul> </li> <li>Cardiac complications in the control group (3201 episodes in 3155 patients) included               <ul style="list-style-type: none"> <li>Acute myocarditis (n=2) and</li> <li>Kawasaki disease (n=8)</li> </ul> </li> </ul>	Potential for underestimation of RSV infection because this was a hospital-based study and patients with relatively mild disease were not included



Nygaard et al., 2023 [27]	<ul style="list-style-type: none"> <li>• Among 133 children receiving mechanical ventilation, 5 had congenital heart disease</li> <li>• Among 87 children with risk factors for severe RSV disease, 5 (6%) required mechanical ventilation due to cardiac complications</li> <li>• Among 46 children, without risk factors for severe RSV, 1 (2%) develop cardiac complications</li> </ul>	Included only hospitalized patients and RSV testing is only performed in the hospital setting in Denmark. The threshold for hospital admissions in the 2021–22 RSV season was likely higher than previous seasons due to overcrowded paediatric departments during the pandemic period and may have resulted in underestimation of the increase in hospital admissions in 2021–22. No detail information on the cardiac complications were provided.
Woodruff et al., 2024 [28]	<ul style="list-style-type: none"> <li>• 56.4% of the 6248 hospitalized adults with laboratory confirmed RSV infection had underlying cardiovascular disease</li> <li>• Weighted estimated period prevalence of experiencing a cardiac event was 22.4% (95% CI, 21.0%–23.7%). <ul style="list-style-type: none"> <li>– Acute heart failure: 15.8% (95% CI, 14.6%–17.0%)</li> <li>– Acute ischemic heart disease: 7.5% (95% CI, 6.8%–8.3%)</li> <li>– Hypertensive crisis: 1.3% (95% CI, 1.0%–1.7%)</li> <li>– Ventricular tachycardia: 1.1% (95% CI, 0.8%–1.4%)</li> <li>– Cardiogenic shock: 0.6% (95% CI, 0.4%–0.8%)</li> <li>– Other acute cardiac event (stress cardiomyopathy, viral cardiomyopathy, myocarditis, pericarditis, and endocarditis): 1.3% (95% CI: 1.0%–1.6%).</li> </ul> </li> <li>• Compared to patients with no history of cardiovascular disease, patients with underlying cardiovascular disease had a greater weighted estimated period prevalence of experiencing an <ul style="list-style-type: none"> <li>– Acute cardiac event of any category (33.0% vs 8.5%; adjusted risk ratio (ARR), 3.51 [95% CI, 2.85–4.32]),</li> <li>– Acute heart failure (25.3% vs 3.5%; ARR, 5.89 [95% CI, 4.30–8.08]), and</li> <li>– Acute ischemic heart disease (10.2% vs 4.1%; ARR, 2.38 [95% CI, 1.84–3.09])</li> </ul> </li> </ul>	Inability to causally attribute acute cardiac events to RSV infection due to a lack of confirmation on the temporality. May focus disproportionately on severe RSV cases that are hospitalized. Lack of data on hospitalized adults without laboratory confirmed RSV, and cardiac events may be underestimated because of limitations of use of diagnostic codes, and there is the potential to include chronic cardiac conditions as acute events.
Wyffels et al., 2020 [29]	<p>During 180 days post-RSV diagnosis,</p> <ul style="list-style-type: none"> <li>• High-risk hospitalized patients developed arrhythmias (51%) and myocardial infarction (19%)</li> <li>• Hospitalized non-high-risk patients developed arrhythmias (18%) and myocardial infarction (14%)</li> <li>• Outpatient high-risk patients developed arrhythmias (29%) and myocardial infarction (6%)</li> <li>• Outpatient non-high-risk patients developed arrhythmias (9%) and myocardial infarction (4%)</li> </ul>	This study used retrospective claims data based on administrative codes rather than clinical tests, potentially causing inaccuracies in identifying RSV cases and complications. Unable to ascertain if complications developed due to RSV or a progression of an underlying disease exacerbated due to RSV.

### Potential Sources of Bias

There are some potential sources of bias in the studies included. In many studies, the definitions of cardiac outcomes were based on hospital records or physician diagnoses, which may introduce variation. Some research relied on retrospective data, increasing the possibility of underreporting mild cardiac events. Additionally, differences in diagnostic methods for RSV such as timing of RT-PCR, might have led to variability in identifying cases. The use of diagnostic codes to identify RSV infection also has the potential for inaccuracies.

### Discussion

This systematic literature review aimed to identify and summarize cardiovascular complications associated with RSV infection. The evidence from the included nine studies consistently suggests that there is considerable burden of cardiovascular complications associated with RSV infection, particularly among hospitalized older adults. Hospitalized adults with pre-existing cardiovascular conditions had an increased risk of an acute cardiac event following RSV infection. These findings demonstrate that RSV is

not only a respiratory pathogen but also significantly impacts cardiovascular health.

Most of the primary studies were conducted in hospitalized patients. The prevalence of cardiovascular complications observed in this study varied considerably across studies, ranging approximately from 8% to as high as nearly 25% in hospitalized adults.<sup>22–24,28</sup> Myocardial infarction, arrhythmias, and heart failure were the most frequently reported cardiovascular complications in adults. Cardiovascular complications occurred in adults without and with pre-existing conditions, including heart diseases and thus consisted of new-onset as well as exacerbation of existing conditions, respectively. Hospitalized adults with pre-existing cardiovascular disease had approximately 2–6 times increased risk of an acute cardiac event after an RSV infection. Hospitalized adults with pre-existing coronary arterial disease also had a higher odds of developing cardiovascular complications. Cardiovascular complications were also observed in non-hospitalized outpatient adults.<sup>29</sup> Given that individuals with pre-existing medical conditions, including cardiac diseases, older adults aged 65 years or older are at increased risk of RSV

infection<sup>22-24,28</sup>, and that the prevalence of chronic diseases increase with age, these findings suggest that adults with pre-existing medical conditions, particularly older adults could benefit from the RSV vaccines in countries with aging population. Indeed, approximately 52% of US adults had at least one chronic condition<sup>30</sup>, and it is estimated that the US population aged 65 years and older will increase by 47% from 2022 (58 million) to 2050 (82 million)<sup>31</sup>, and older adults would likely benefit from the RSV vaccines in reducing the burden of cardiac and other complications associated with RSV infection.

Cardiovascular complications were less prevalent in children compared to adults. This is not surprising as severe RSV predominantly results in respiratory complications such as bronchiolitis and pneumonia in infants and young children<sup>32</sup>. Similar to adults, children without and with pre-existing medical conditions, including heart diseases developed cardiovascular complications following an RSV infection.

However, there are several limitations to consider when interpreting these findings. Many studies utilized retrospective designs or relied on administrative databases and diagnostic codes, which could potentially introduce inaccuracies. Differences in laboratory methods and timing of RSV diagnosis may also have affected the identification and reporting of RSV cases, leading to variability in reported outcomes. There was a lack of data on the burden of cardiovascular complications following RSV infection according to the social determinants of health. In addition, nearly all of the studies focused on hospitalized patients. Only one primary study included both inpatient and outpatient, and reported cardiovascular complications. As such, RSV cases with cardiovascular complications that did not require hospitalization were not captured, and the true burden of cardiovascular complications following an RSV infection of any level of severity is likely higher than the burden identified in the hospitalized patients.

### Strengths and Limitations

The strength of this systematic review includes the comprehensive search of multiple databases, clear inclusion and exclusion criteria, and systematic data extraction, all of which help ensure reliability and transparency. However, the review also has some limitations by restricting the search to English-language studies may have excluded potentially relevant studies published in other languages. Additionally, the studies included were primarily from high-income settings, limiting the generalizability of the findings to other populations.

### Conclusion

Despite these limitations, the consistency of the reported burden of cardiovascular complications associated with RSV infection across various settings and study designs strengthens confidence in the findings. Future research should focus on standardized RSV infection detection by using diagnostic approaches, such as consistent use of RT-PCR testing within a defined timeframe after symptom onset; more robust prospective designs, such as long-term cohort studies tracking cardiovascular outcomes post-RSV infection; and examining broader populations, including diverse socioeconomic settings, to improve understanding of RSV-related cardiovascular complications. Individuals at high-risk of RSV infection and cardiovascular complications following an RSV infection, particularly younger children and older adults could benefit from targeted preventive strategies such as RSV vaccination.

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