

RSV nell'adulto: nuove prospettive

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Segni e sintomi di infezione da VRS negli adulti

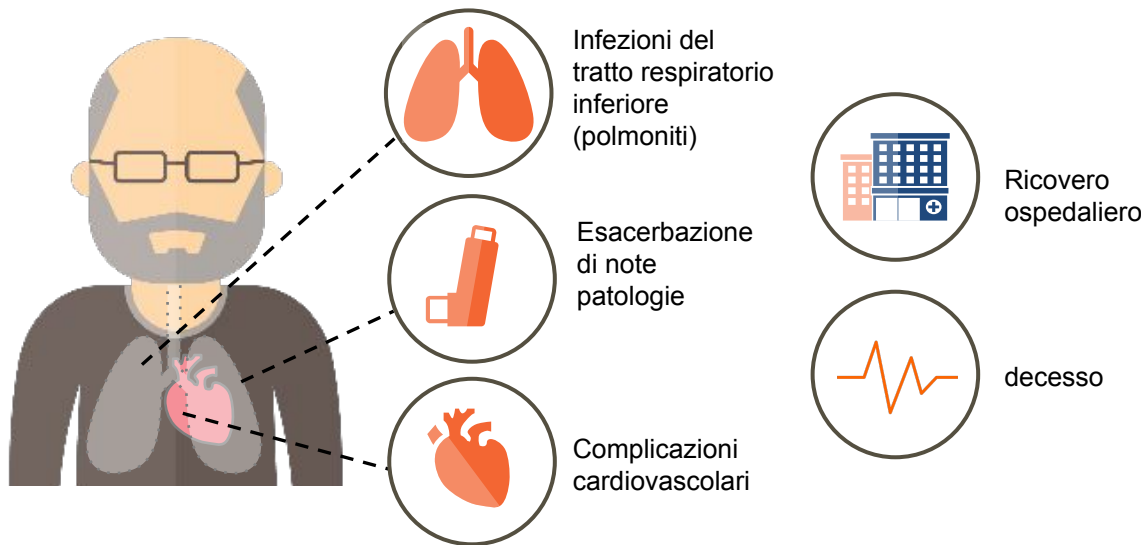
Infezione da RSV è tipicamente lieve, ma può determinare serie complicazioni

Tipicamente le infezioni da VRS negli adulti sani determinano sintomi lievi simil-influenzali^{1,2}



I sintomi possono essere simili a quelli di altri patogeni respiratori^{2,3}

Tuttavia, il VRS può determinare gravi condizioni^{1,3}:

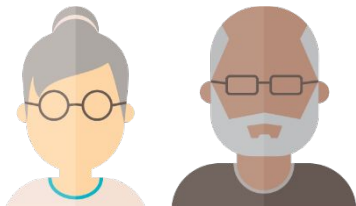


1. Centers for Disease Control and Prevention (CDC), 2023. RSV in older adults and adults with chronic medical conditions.

<https://www.cdc.gov/rsv/high-risk/older-adults.html>; 2. Nam HH and Ison MG. BMJ 2019;366:l5021; 3. Branche AR, Falsey AR. Drugs Aging 2015;32:261–269

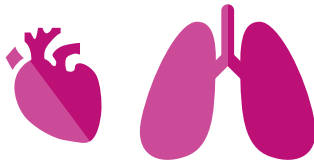
Fattori di rischio per severa malattia associata a VRS negli adulti

Il rischio di una severa malattia associate a VRS aumenta con l'età e con certe patologie



Età avanzata^{1,2}

Specialmente per coloro con
età ≥60 anni



Comorbidità^{1,3,4}

Gli adulti a **rischio aumentato**
includono coloro con certe
comorbidità
(asma, BPCO, CHF, CAD, diabete, CKD)



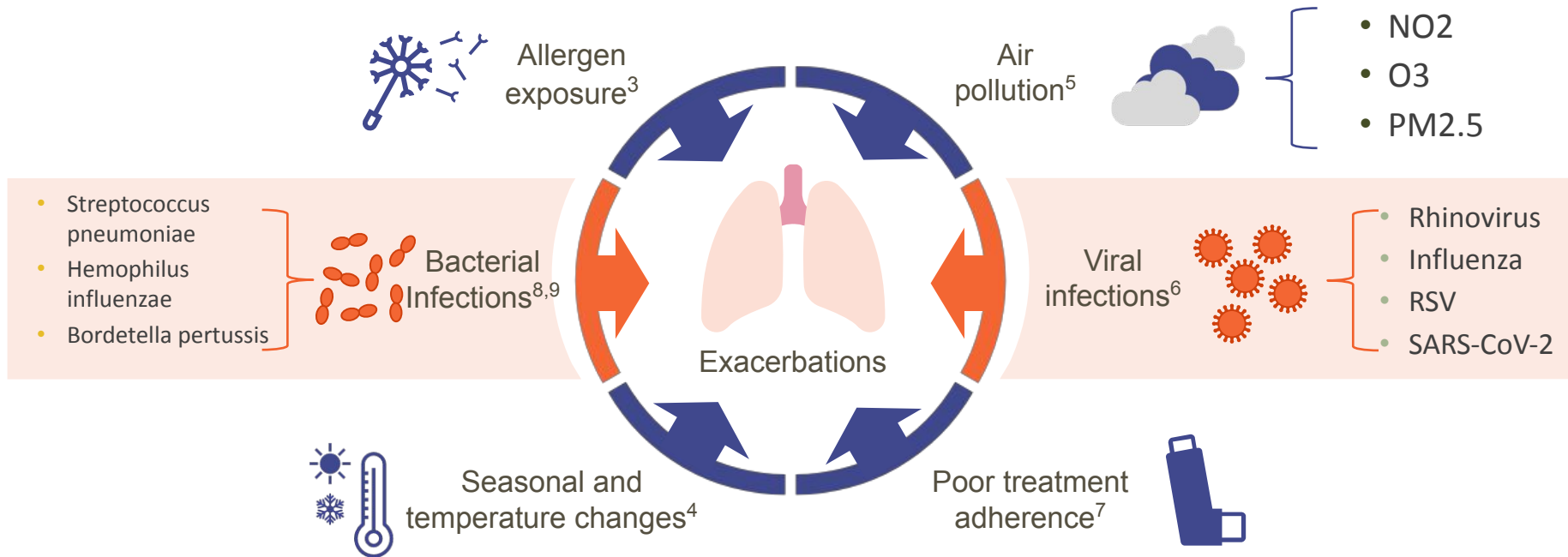
**Alterazioni dello stato
immunitario¹**

Gli adulti con **sistema
immunitario alterato** sono ad
aumentato rischio di una severa
malattia da VRS

CAD, coronary artery disease; CHF: congestive heart failure; CKD, chronic kidney disease;

1. Centers for Disease Control and Prevention (CDC), 2022. RSV in older adults and adults with chronic medical conditions. <https://www.cdc.gov/rsv/high-risk/older-adults.html> (accessed February 2023); 2. Belongia EA et al. *Open Forum Infect Dis* 2018;27;5:ofy316; 3. Branche AR et al. *Clin Infect Dis* 2022;74:1004–1011; 4. Wyffels V et al. *Adv Ther* 2020;37(3):1203–1217

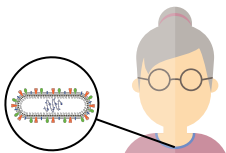
Infections are among the most common contributors to respiratory disease exacerbations^{1,2}



AECOPD, acute exacerbation of COPD; COPD, chronic obstructive pulmonary disease

1. GOLD. Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease, 2023 Report. 2. Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2023 3. Singh AM, Busse WW. *Thorax* 2006;61:809–816; 4. Jenkins CR *et al. Eur Respir J* 2012;39:38–45; 5. Hansel NN, *et al. The Effects of Air Pollution and Temperature on COPD. J Chron Obstruct Pulmon Dis.* 2016;13:372–9 6. Jang JG, *et al. Int J Chron Obstruct Pulmon Dis.* 2021;16:1265–73;; 7. Williams LK *et al. J Allergy Clin Immunol* 2011;128:1185–1191 8. Moghoofoei M, *et al.. Infection.* 2020;48:19–35; 4. Wilkinson TMA, *et al.. J Chron Obstruct Pulmon Dis.* 2021;18:341–8.

Peso clinico annuale negli adulti in Europa



RSV-ARI incidence, 2019

>3 million cases of RSV-ARI^{*,1}



Hospitalization for RSV-ARI, 2019

~274,000 hospitalizations^{*,1}



In-hospital case fatality rate, 2019

~20,000 deaths^{*,1}

An unknown number of people
die outside of hospital¹



RSV is currently not covered by the European community network for surveillance of communicable diseases²

The ECDC currently collects data on RSV and has launched an integrated surveillance strategy for respiratory diseases in the EU/EEA countries³

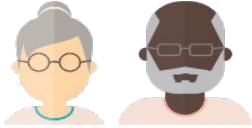
^{*}Calculated using the European population aged ≥60 years old in 2019¹

ARI, acute respiratory infection; EEA, European Economic Area; ECDC, European Centre for Disease Prevention and Control; EU, European Union

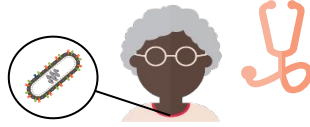
1. Savic M et al. *Influenza Other Respir Viruses* 2023;17(1):e13031; 2. ECDC, 2015. Workshop on burden of RSV disease in Europe November 23–24. <https://www.ecdc.europa.eu/sites/portal/files/media/en/press/events/Documents/Meeting%20report%20ECDC%20RSV%20surv%20and%20burden%20of%20disease%20workshop%2023-24%20Nov.pdf> (accessed February 2023); 3. ECDC, 2022. Communicable disease threats report, week 46, November 13–19. <https://www.ecdc.europa.eu/en/publications-data/communicable-disease-threats-report-13-19-november-2022-week-46> (accessed February 2023)

Elevato peso di VRS negli adulti

Estimated annual burden of RSV infection among adults aged ≥ 65 years in the USA¹



3–7% of older adults experience RSV infection¹



**Hospitalization for RSV infection
>177,000 hospitalizations¹**



**Death due to RSV infection
14,000 deaths^{*,1}**

Systematic literature review and meta-analysis estimated the annual burden of RSV-ARI among those aged ≥ 60 years²

Incidence

1.62% (95% CI: 0.84, 3.08)

Hospitalization

0.15% (95% CI: 0.09, 0.22)

In-hospital case fatality rate

7.13% (95% CI: 5.40, 9.36)

291,354 (151,561 – 555,905)
cases of RSV-ARI in Italy**

26,162 (16,960 – 40,416)
hospitalizations in Italy**

1,866 (917-3,783)
deaths in Italy**

*Based on 8% death rate for hospitalized patients with RSV infection¹ **Calculated using the European population aged ≥ 60 years old in 2019 ARI, acute respiratory infections;
1. Falsey AR et al. *N Engl J Med* 2005;352:1749–1759; 2. Savic M et al. *Influenza Other Respir Viruses* 2023;17(1):e13031

Morbidity e mortalità nei pazienti adulti ospedalizzati con VRS

A retrospective cohort study of hospitalized adults
(mean age, 75 years) with RSV in Hong Kong (N=607)

Study population

87.3% had ≥ 1 comorbidity

Major systemic comorbidity
(excluding chronic respiratory
disease):*

74.0%

Chronic lung disease:†

35.6%

Outcomes



Crude all-cause mortality:

- **9.1%** (n=55) within 30 days
- **11.9%** (n=72) within 60 days

Direct causes of death:

- Pneumonia (n=48)
- COPD exacerbation (n=5)
- Acute CV events (n=12)
- Underlying medical conditions complicated by pneumonia/sepsis (n=7)



- **11.1%** (n=67) required ventilatory support
- **67.9%** (n=412) required supplemental oxygen



Mean duration of hospitalization of survivors: **12 days**

RSV can cause severe lower respiratory complications in older adults, resulting in respiratory failure, prolonged hospitalization, and high mortality

*Congestive heart failure; cerebrovascular, neoplastic, and chronic liver or renal diseases; other chronic cardiovascular and neurologic conditions (except hypertension); diabetes mellitus; autoimmune disorders; immunocompromised; †Chronic obstructive pulmonary disease, asthma, bronchiectasis, and pulmonary fibrosis
COPD, chronic obstructive pulmonary disease; CV, cardiovascular
Lee N *et al. Clin Infect Dis* 2013;57(8):1069–1077

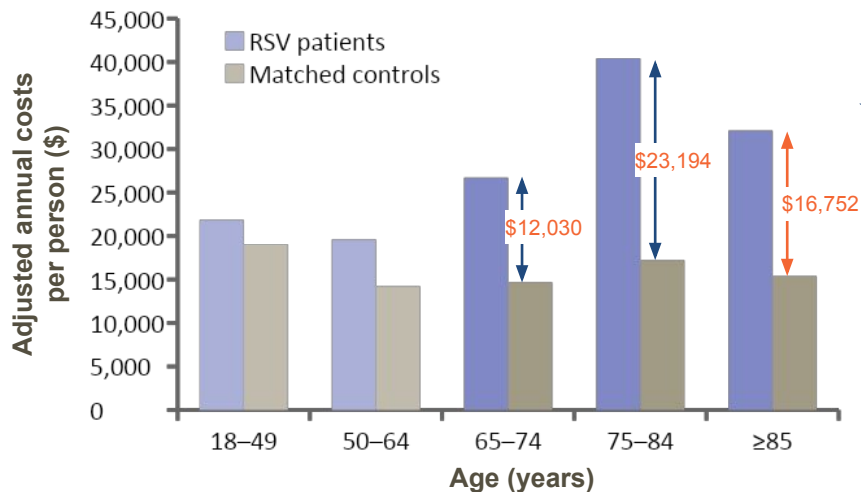
Peso economico del VRS negli adulti

RSV in older adults causes a sizeable burden on healthcare systems and incurs socioeconomic costs

A retrospective case–control database analysis quantified RSV-related healthcare resource use and costs by age group¹

N=11,432 patients with RSV were matched 1:1 with non-RSV controls, matched for age, sex, region and health plan; 2012–2013*

Annual healthcare costs for adults with RSV vs matched controls



Patients with RSV had significantly higher healthcare resource use than controls for all age groups¹

Older adults aged ≥65 years showed the greatest difference in costs incurred between RSV and non-RSV groups¹



A recent study assessed outcomes associated with RSV infections in US adults aged ≥60 years during one RSV season

Annual direct RSV-related medical cost was estimated to be

\$1.52–2.99 billion²

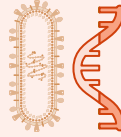
1. Amand C et al. *BMC Health Serv Res* 2018;18:294; 2. Herring WL et al. *Vaccine* 2022;40:483–493

Limited RSV surveillance system contribute to the underestimation of disease burden¹

Diagnosis, management, and prevention of RSV infection

Diagnosis

- Symptoms of RSV infection are nonspecific and may be indistinguishable from those of other respiratory infections. Testing is needed to confirm diagnosis⁶
- Testing and diagnosis of RSV is not routinely considered for adults with influenza-like illness⁷



Management

- Currently, there is no specific treatment available for RSV in adults⁸
- The mainstay of therapy for acute infection is supportive care^{6,8}

Prevention



- Vaccines have recently become available for adults ≥ 60 years of age^{*2-5}
- Previously, non-pharmaceutical infection prevention and control measures were the best protection against RSV^{9,10}

*As of July 2023, RSV vaccines for older adults have been approved by the US Food and Drug Administration (Arexvy, GSK; Abrysvo, Pfizer), and authorized by the European Commission (Arexvy, GSK) and the UK's Medicines and Healthcare products Regulatory Agency (Arexvy, GSK).
1. National Foundation for Infectious Diseases. Respiratory syncytial virus in older adults: a hidden annual epidemic. 2016. Available at: <https://www.nfid.org/wp-content/uploads/2019/08/rsv-report.pdf>. Accessed November 2022; 2. Food and Drug Administration (FDA), 2023. Arexvy Prescribing Information (PI). <https://www.fda.gov/media/167805/download> (accessed June 2023); 3. Food and Drug Administration (FDA), 2023. Abrysvo Prescribing Information (PI). <https://www.fda.gov/media/168889/download> (accessed June 2023); 4. European Medicines Agency (EMA), 2023. Arexvy. <https://www.ema.europa.eu/en/medicines/human/EPAR/arexvy> (accessed June 2023); 5. Medicines & Healthcare products Regulatory Agency (MHRA), 2023. Arexvy Summary of Product Characteristics. <https://mhraproducts4853.blob.core.windows.net/docs/e3ae9af503f9e9824a7d1d40538536337caafaf8> (accessed July 2023); 6. Centers for Disease Control and Prevention (CDC), 2022. RSV for Healthcare Providers. <https://www.cdc.gov/rsv/clinical/index.html> (accessed February 2023); 7. Branche AR. Clin Infect Dis 2019;69:204–206; 8. Kodama F et al. Infect Dis Clin North Am 2017;31:767–790; 9. Centers for Disease Control and Prevention (CDC), 2022. RSV prevention. <https://www.cdc.gov/rsv/about/prevention.html> (accessed June 2023); 10. Nam HH and Isom MG. BMJ 2019;366:l5021

Le infezioni virali sono il fattore di rischio principale del peggioramento di asma e BPCO

COPD



Longer hospitalization¹⁻³

11.6 ± 0.6 days for infective* exacerbations vs 8.8 ± 0.8, $P < 0.02$ for non-infective exacerbations³



Accelerated lung function decline^{1,3}

Greater decreases in FEV₁ (0.25 ± 0.03 L vs 0.12 ± 0.04 L, $P < 0.05$) in infective* vs non-infective exacerbations³



Greater hypoxemia^{2,3}

A trend for a greater decrease in Pa_{O₂} (15.3 ± 1.35 vs. 11.92 ± 1.86 mm Hg, $P = 0.078$) in infective* vs non-infective exacerbations³



Greater airway inflammation³⁻⁵

Higher airway eosinophils and serum IL-6 levels in virus-associated exacerbations than non-viral exacerbations, $P = 0.064$ ^{3,4}

Asthma



Hospital admissions⁶

RSV infection accounted for 7.2% of asthma hospitalizations in adults ≥65 years of age⁶



Enhanced responsiveness to allergens^{7,8}

8/10 vs 1/10 patients had FEV₁ decline after exposure to a combination of allergen and rhinovirus vs allergen alone⁷



Altered antiviral immune response in asthmatics is associated with asthma worsening^{6,7,9,10}

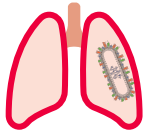
Positive association between rhinovirus load and CD45+, CD68+, CD20+, neutrophils and eosinophils at 4 days post-infection¹⁰

*Viral and/or bacterial infection

CD, cluster of differentiation; COPD, chronic obstructive pulmonary disease; FEV₁, forced expiratory volume in 1 second; IL, interleukin; Pa_{O₂}, partial pressure of oxygen in arterial blood

1. Linden D et al. *Eur Respir Rev* 2019;28:180063; 2. Mohan A et al. *Respirology* 2010;15(3):536–426; 3. Papi A et al. *Am J Respir Crit Care Med* 2006;173(10):1114–1121; 4. Seemungal T et al. *Am J Respir Crit Care Med* 2001;164(9):1618–1623; 5. Aghapour M et al. *Am J Respir Cell Mol Biol* 2018;58:157–169; 6. Westerly BD, Peebles RS. *Immunol Allergy Clin North Am* 2010;30:523–539; 7. Adeli M et al. *J Family Med Prim Care* 2019;8(9):2753–2759; 8. Ojanguren I et al. *Arch Bronconeumol*. 2022;58(9):632–634; 9. Hewitt R et al. *Ther Adv Respir Dis* 2016;10:158–174; 10. Zhu J et al. *Chest*. 2014;145(6):1219–1229

L'infezione da VRS può essere una importante causa di riacutizzazioni di asma e BPCO



RSV has been detected in **10%** of acute exacerbations of COPD¹



RSV accounted for:

- **11.4%** of hospitalizations for COPD, and
- **7.2%** of hospitalizations for asthma in prospective cohorts including healthy adults aged ≥ 65 years and adults with chronic lung or heart disease²



Among adults, aged ≥ 18 years, hospitalized with RSV-ARI across 12 countries (N=238):³

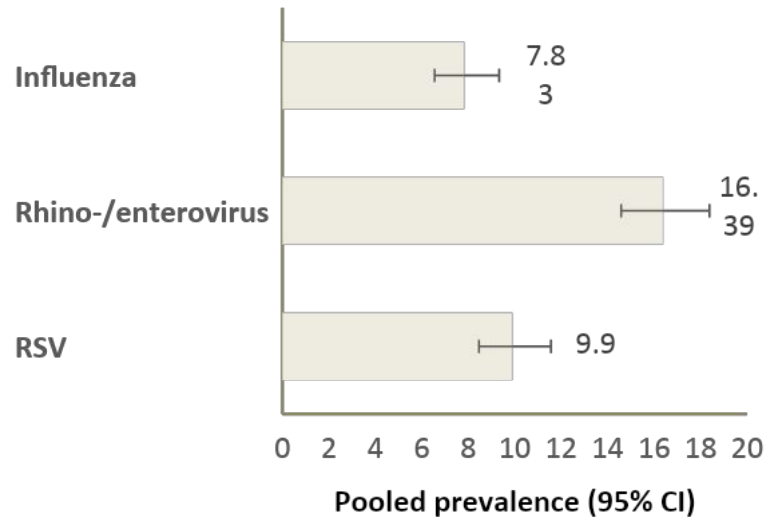
- **26%** had COPD exacerbations
- **13%** had asthma exacerbations

ARI, acute respiratory tract infections; COPD, chronic obstructive pulmonary disease.

1. Zwaans WA *et al.* *J Clin Virol* 2014;61:181–188; 2. Falsey AR *et al.* *N Engl J Med* 2005;352:1749–1759; 3. Falsey AR *et al.* *Open Forum Infect Dis* 2021;8(11):ofab491.

Virus Respiratori durante la riacutizzazioni di BPCO

Una revisione sistematica sulla prevalenza dei virus respiratori nei pazienti con una riacutizzazione di BPCO in 19 studi (N=1728)



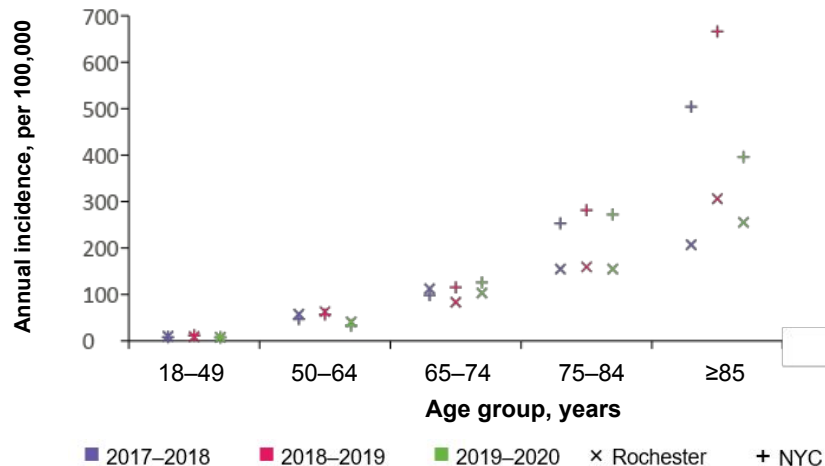
Virus	Pooled prevalence (95% CI)	
	Upper respiratory airways	Lower respiratory airways
Influenza	5.43 (4.25, 6.91)	9.88 (7.71, 12.58)
Rhino-/enterovirus	13.50 (11.67, 15.57)	16.50 (13.74, 19.69)
RSV	9.02 (7.49, 10.83)	11.93 (9.54, 14.81)

Rinovirus, VRS e influenza sono più frequentemente rilevati nelle basse vie respiratorie confrontati con i campioni rilevati nelle alte vie respiratorie

Il rischio di ospedalizzazioni associate al VRS aumenta con l'età e le comorbidità

A large prospective study estimated incidence of RSV-associated hospitalization in two regions of New York State, USA, 2017–2020. N=1099 cases

Incidence of RSV-associated hospitalization by age group and season

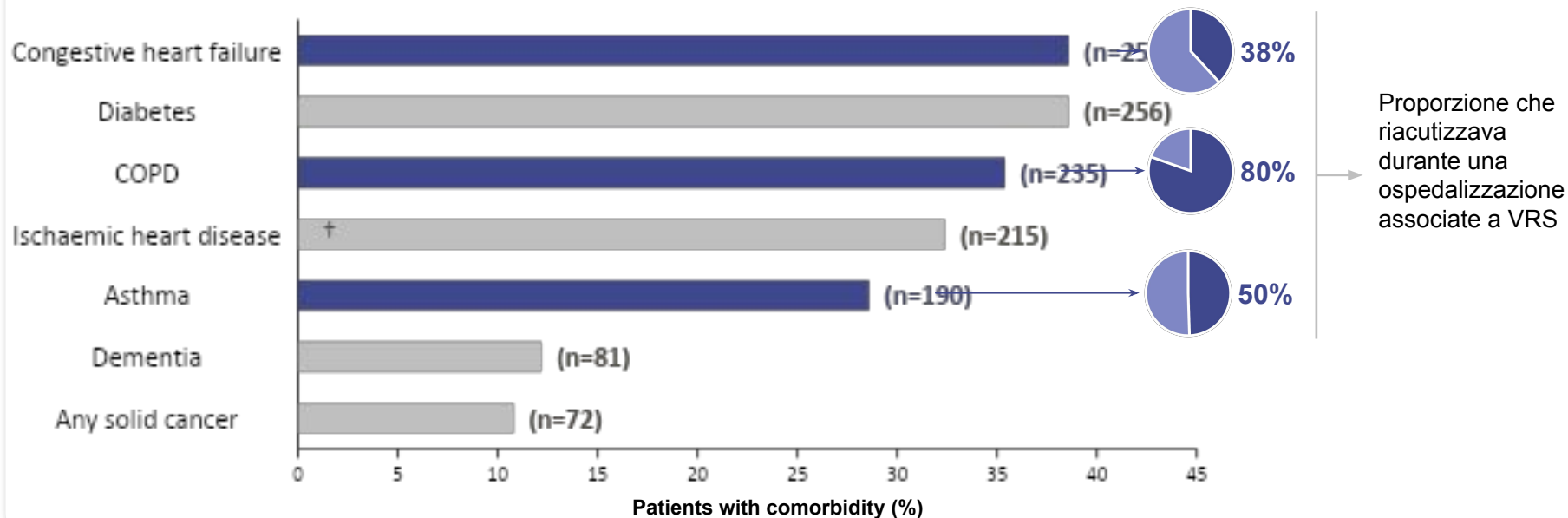


Hospitalization rates for RSV were higher in adults aged ≥50 years with comorbidities

Comorbidity	Incidence rate ratio*
Asthma	2.3–3.6
COPD	3.5–13.4
CAD	3.7–6.5
CHF†	4.0–7.6
Diabetes	2.4–6.4

Condizioni patologiche sottostanti sono più comuni negli adulti ospedalizzati con VRS

Comorbidities among patients aged ≥ 60 years hospitalized with RSV in Kaiser Permanente Southern California, USA, 2011–2015 (N=664)*

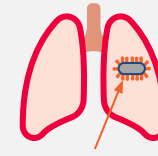
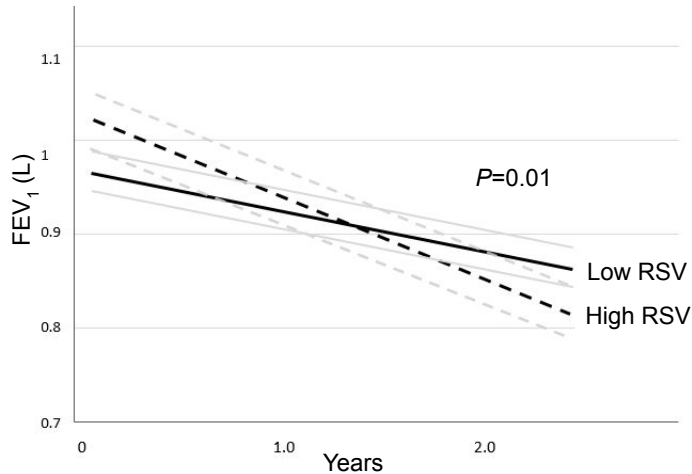


*Comorbidities were present in the year prior to hospital admission; †COPD, chronic bronchitis, or emphysema
Tseng HF *et al. J Infect Dis* 2020;222:1298–1310

Infezione persistente da VRS nei pazienti BPCO è associate con un declino accelerato della funzionalità respiratoria

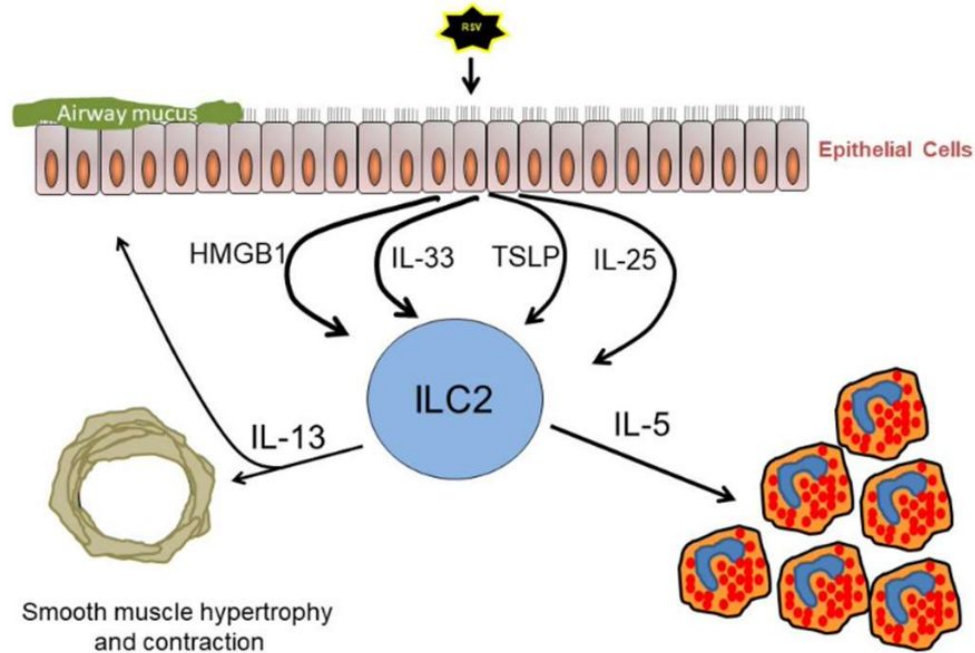
Uno studio prospettico ha valutato le conseguenze del VRS nei pazienti con BPCO in due anni (N=74)

Relazione tra diagnosi di VRS e decline di FEV_1 nel period di studio*

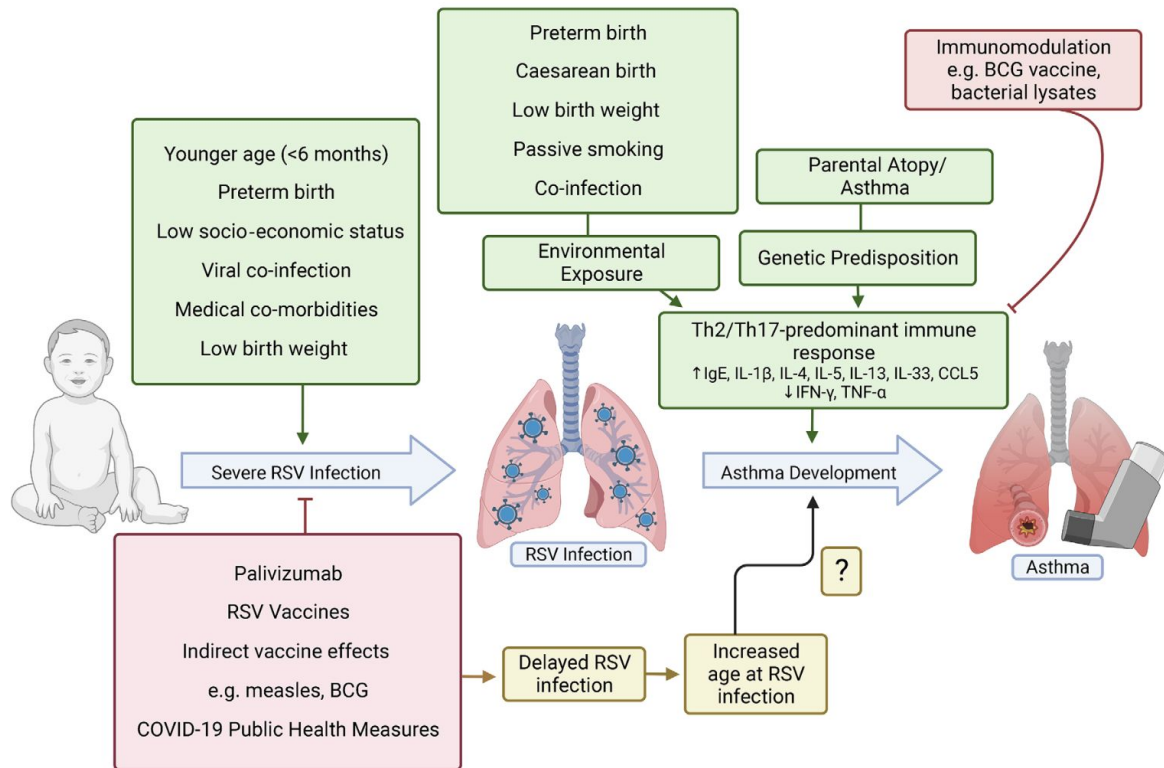


Test ripetutamente positivi per VRS (infezione cronica) sono associati con un più rapido declino del FEV_1 e più elevate parametri infiammatori nei pazienti con BPCO stabile

Innate type 2 immune response to respiratory syncytial virus (RSV)

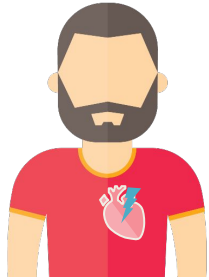


Respiratory syncytial virus, recurrent wheeze and asthma



Correlazione tra infezioni respiratorie e malattie cardiovascolari

Le infezioni virali respiratorie possono esacerbare malattie cardio-vascolari esistenti e stimolare nuovi eventi cardiovascolari¹



People with chronic CV diseases are at increased risk of severe outcomes from respiratory tract infections²⁻⁴



ARIs are associated with CV complications, such as CHF, myocardial ischemia and infarction, and atrial fibrillation^{1,5}



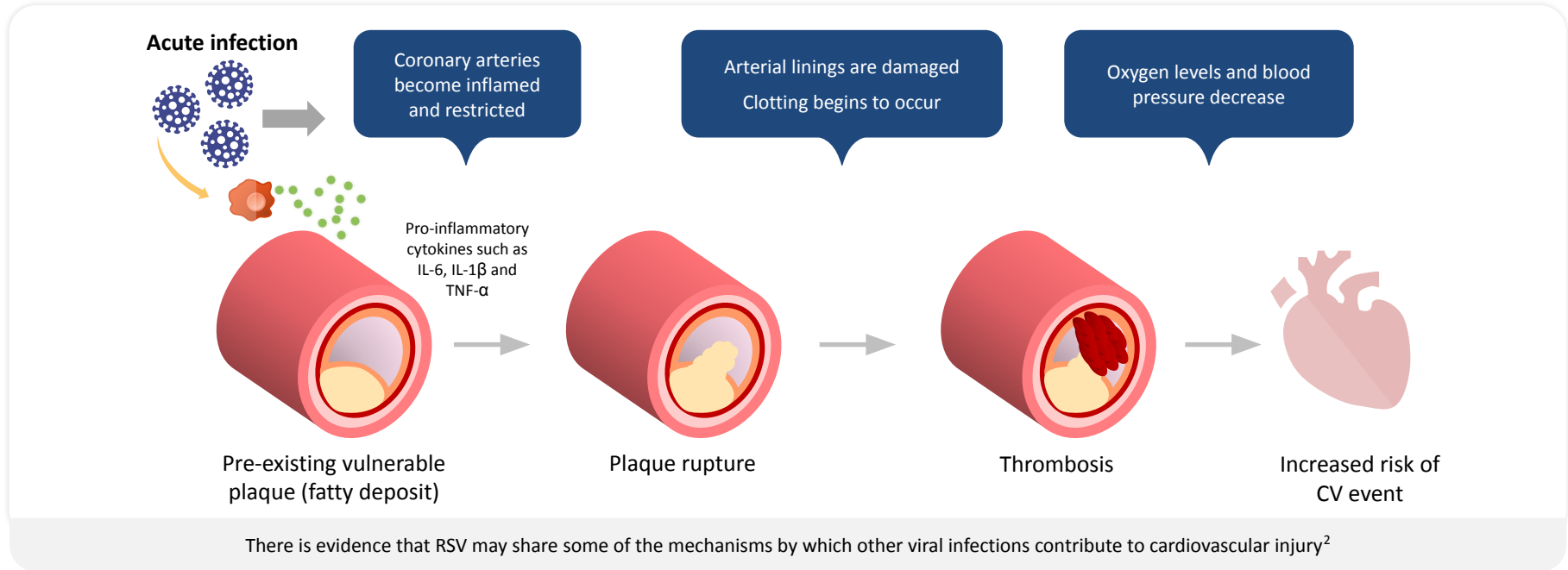
Heart failure, myocardial infarction and atrial fibrillation cause significant, long-term, morbidity and mortality^{1,7-9}

ARI, acute respiratory infection; CHF, congestive heart failure; CV, cardiovascular.

1. Franczuk P et al. *Biomedicine* 2023;11(1):71; 2. Centers for Disease Control and Prevention (CDC), 2023. Older adults are at high risk for severe RSV. <https://www.cdc.gov/rsv/factsheet-older-adults.pdf>; 3. Branche AR et al. *Clin Infect Dis* 2022;74:1004-1011; 4. Rosenthal N et al. *JAMA Netw Open* 2020;3(12):e2029058; 5. Ivey KS et al. *J Am Coll Cardiol* 2018;71(14):1574-1583; 6. Centers for Disease Control and Prevention (CDC), 2022. Flu & People with Heart Disease or History of Stroke. <https://www.cdc.gov/flu/highrisk/heartdisease.htm>; 7. Centers for Disease Control and Prevention (CDC), 2023. Heart disease. https://www.cdc.gov/heartdisease/heart_failure.htm; 8. Centers for Disease Control and Prevention (CDC), 2022. Heart attack symptoms, risk, and recovery. https://www.cdc.gov/heartdisease/heart_attack.htm; 9. Centers for Disease Control and Prevention (CDC), 2022. Atrial fibrillation. https://www.cdc.gov/heartdisease/atrial_fibrillation.htm. All URLs accessed June 2023.

L'inflammatione sistemica dovuta al VRS può stimolare il rilascio di citochine pro-infiammatorie¹⁻³

La risposta infiammatoria può portare alla rottura di placche arteriose ed aumentare il rischio di sindrome coronarica acuta¹



1. Corrales-Medina VF *et al. Lancet Infect Dis* 2010;10:83–92; 2. Ivey KS *et al. J Am Coll Cardiol* 2018;71:1574–1583; 3. Franczuk P *et al. Biomedicines* 2023;11(1):71

Conclusioni: VRS e patologie polmonari



I pazienti anziani con BPCO e gli asmatici presentano un aumentato rischio di severa malattia da VRS, che causa una risposta infiammatoria prevalentemente Th2



Una elevata proporzione di adulti ospedalizzati per VRS presentano una riacutizzazione di asma o BPCO



Una infezione persistente da VRS è associata con un declino di funzionalità respiratoria e una più elevata infiammazione delle vie aeree nei pazienti con BPCO