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ABSTRACT

Respiratory syncytial virus (RSV) is an important cause of respiratory illness. While most attention is paid to childhood infection, the RSV burden in adults ≥ 60 y should also be considered. In Brazil, this is generally underrecognized, where greater focus is toward other respiratory pathogens. This article presents insights from a multidisciplinary panel gathered to review epidemiologic data and current diagnostic approaches to RSV in Brazil (and their limitations) and develop communication strategies to improve knowledge and awareness. National surveillance data indicate a steady increase in cases of RSV-related severe acute respiratory illness (RSV-SARI) in those aged ≥ 60 y in recent years, with high fatality rates ($>30\%$). Routine RSV testing in older individuals with respiratory symptoms is relatively low. Educational activities targeted toward health-care professionals and the general public are critical to raising awareness of the importance of RSV in older individuals, particularly as protective vaccines are now available.

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Introduction

Respiratory syncytial virus (RSV) is a leading cause of morbidity and mortality in children <5 y of age, especially in younger infants.^{1–3} However, RSV is being increasingly recognized as an important cause of acute, and often severe respiratory illness in older adults ≥ 60 y of age, where hospitalization and mortality may be substantial.^{4–8} Prospective community-based studies from the United States (US) and Europe indicate that symptomatic RSV illness occurs in between 3–7% of older adults each year.^{9–11} As many as 25% of older adults with RSV infection will require hospitalization,⁷ and in high-income countries, RSV accounts for 4–12% of all acute respiratory infection (ARI) hospitalizations in adults ≥ 60 y of age (and broadly comparable to those reported for influenza).^{12–14} RSV disease severity is greater in individuals with comorbidities (cardiopulmonary disease, diabetes, immunocompromised), and hospitalization rates are 3–10-fold higher in such high-risk patients, and where RSV infection is associated with worsening of underlying cardiopulmonary disease.^{7,15,16} RSV-associated mortality is also substantial in older adults, both in the acute phase and over the longer term, and again is far

greater in those with comorbidities.^{16–18} Furthermore, it is generally recognized that estimates for morbidity and mortality are likely to underestimate the true burden.^{19,20}

Despite this, the role of RSV as an important respiratory illness and a frequent cause of severe acute respiratory infection (SARI) in older adults, and it remains relatively underrecognized, both by clinicians and by the broader lay public, with a general perception that RSV is a pediatric infection.^{21–23} For older adults presenting with any SARI in the clinical setting, more attention is paid toward influenza diagnosis (and obviously to coronavirus disease 2019 [COVID-19] disease in recent years) with the possibility of RSV considered less likely and infrequently investigated.²⁴ This perception is generally apparent in most countries, including Brazil, and indeed across Latin America, where studies focusing on RSV in older adults are relatively sparse.^{25–27} At a broader public health level, influenza in older adults also gathers greater attention than RSV, as routine vaccination of older adults is embedded within national immunization policy, and where broader routine surveillance allows assessment of the impact and benefits of such policies.^{28–30} As we describe below, RSV case

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notifications in older adults are increasing within Brazil,³¹ within a broader pattern of substantial increases in RSV notifications in recent years (although in part, this also reflects expanded testing for viral respiratory pathogens initiated during the COVID-19 pandemic). Nevertheless, routine RSV testing in older adults is relatively low, although, to some extent this is a global pattern, rather than one specific to Brazil.^{21,22,24}

Such considerations highlight the need to raise awareness of the significance of RSV infection in Brazilian older adults to health-care professionals and the general public. Indeed, this has been highlighted nationally, with a parliamentary health committee public hearing in October 2023 regarding RSV epidemiology and the need for greater awareness.³² This is particularly important given the recent development of effective RSV vaccines for use in individuals ≥ 60 y of age,^{33–35} and their recent approval for use in Brazil.^{36,37} To this aim, a multidisciplinary panel was formed to provide insights into the current status of RSV involving older adults within Brazil, including the potential benefits of protective vaccination. The present paper represents the major findings and insights from these discussions.

Methods

A multidisciplinary panel was established comprising individuals with experience and expertise across a range of specialties (infectious disease, pulmonologists, geriatrics, pediatrics, gynecology, epidemiology and immunization) from across Brazil. The panel convened for a one-day meeting in Sao Paulo on July 21, 2023, to review RSV pathophysiology and immunology, recent surveillance data, and the significance of comorbidities in RSV outcomes in older adults. The panel discussion was organized by GSK. As part of this activity, a specific retrospective analysis of RSV-SARI notifications within the Sistema de Informação da Vigilância Epidemiológica da Gripe (SIVEP-Gripe) database for 2020–2022 was performed, with some data subsequently presented in September 2023 at a national conference.³⁸ The panel then discussed and provided perspectives on perceptions of RSV risk and diagnostic testing within Brazil and strategies that may help increase awareness of RSV disease among health-care professionals and the lay public.

This project was conducted through a review of publicly available literature and anonymized datasets and did not involve specific human participants or any identifiable data. Institutional review board approval and informed consent were not required.

Overview of RSV infection

RSV is a negative-sense single-stranded RNA capsulated enveloped pneumovirus belonging to the *Paramyxoviridae* family within the broader *Mononegavirales* order.^{39,40} Virulence is associated with two key capsular glycoproteins. The G protein facilitates attachment to respiratory epithelial cells, while the F protein mediates cell entry and also fusion of the virus envelope with the host cell membrane and adjacent cell–cell fusion of the virus envelope with the host cell membrane and adjacent cell–cell fusion, generating multinucleated

syncytia, hence the virus name. The G protein shows genetic and antigenic diversity, which underlies the classification of RSV into RSV-A and RSV-B groups/subtypes. Both RSV-A and B can co-circulate, although in general, for most settings (continental, national or regional level), one subtype will generally predominate over an individual season.⁴¹ For example, national serological data for Brazil indicate that RSV-B predominated in 2016 and 2017, while in 2018, RSV-A was predominant.⁴² More recently, data indicate that RSV-A was the most frequent form identified within samples in Sao Paulo in 2021, whereas RSV-B predominated in 2022, with a further switch to RSV-A being predominant in 2023.^{43,44} Whether these subtypes are associated with differences in disease severity is open to debate, and while some studies indicate that RSV-A may cause more severe disease, this is not a consistent finding.^{42,45} In contrast to the G protein, the F protein is highly conserved (across A and B subtypes) and is the target antigen for RSV vaccines developed for older adults,^{34,35} and also for passive immunization treatments for infants.⁴⁶

RSV infection shows a seasonal pattern, typically peaking in temperate countries in the winter months.⁴⁷ In Brazil, which spans a vast geographical region and differing climates (from temperate to sub-tropical), this seasonal pattern is less pronounced, with some variations across the country. However, the general pattern is for RSV activity to begin from early March onwards, peaking from May to July.^{42,47,48} (Figure 1). As we discuss below, these usual patterns, globally and within Brazil, were disrupted by declines in seasonal respiratory infections (both influenza and RSV cases) in the first year of the COVID-19 pandemic associated with nonpharmaceutical interventions (lockdowns and school/workplace closure, physical distancing, reduced movement and social mixing, mask policies, and increased hand hygiene) implemented to mitigate against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) transmission.^{49–53} Some elements of under-testing for other respiratory pathogens due to limited diagnostic capacity during the COVID-19 pandemic may also have contributed to the decline in RSV case numbers.⁵⁴ As such measures relaxed, RSV infection resurged, with more atypical seasonal patterns. Similar changes were observed globally in both Northern and Southern temperate zones.^{51,52,55}

The RSV virus is highly contagious, chiefly transmitted by aerosol/droplet infection, direct contact with infected individuals and indirect contact via contaminated objects and surfaces. Transmission between infected individuals, including children of different age-groups (siblings or at school) and between children and adults (at home or within the community) is poorly understood.⁵⁶ Neither is transmission within the hospital setting (between and among patients and health-care workers), although nosocomial infection and hospital outbreaks are well reported, as are outbreaks within geriatric long-term care facilities.^{57,58}

Following exposure, symptoms initially manifest after 3–4 d and are broadly similar to those seen with influenza or other influenza-like illnesses (ILIs); (cough, nasal congestion and rhinorrhea, wheezing and sore throat). In healthy younger adults, RSV typically manifests as a mild upper respiratory tract infection, resolving within 7–10 d and rarely causing severe disease.⁵⁹ Clinical progress is quite different at both

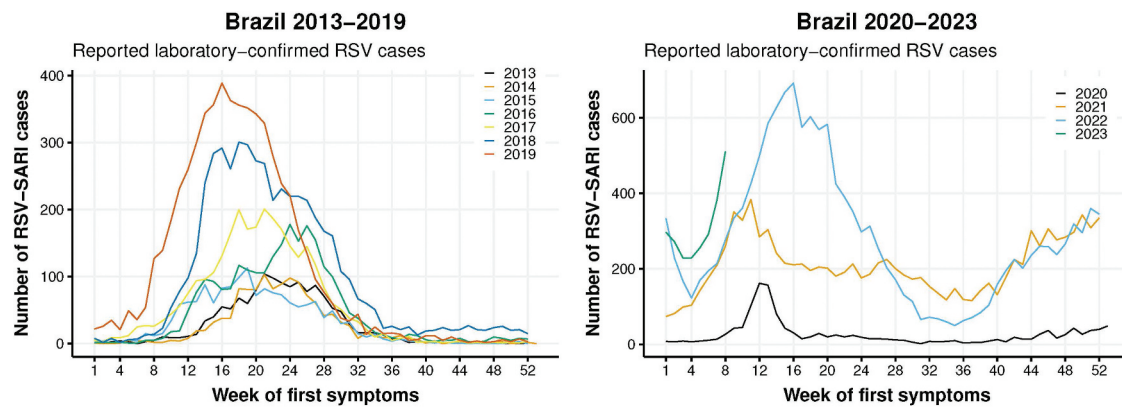


Figure 1. Overview of RSV-SARI notifications and seasonal patterns in Brazil since 2013. Data reflect weekly number of RSV positive SARI cases reported in the SIVEP-Gripe database for 2013–2019 and 2020–2022 (and early 2023). The broad pattern is that of an increasing number of cases reported each year. Prior to COVID-19, RSV activity typically begins from March onwards, peaking through May to June. In 2020, case numbers fell substantially, with a resurgence in case numbers in 2021 and particularly 2022 onwards. RSV activity in these years shows a different pattern, with an initial peak in March/April followed by a subsequent increase in the latter part of the year. Abbreviations: COVID-19; coronavirus disease 2019; RSV; respiratory syncytial virus; SARI: severe acute respiratory infection

ends of the age-spectrum. In young children, and especially infants, lower respiratory tract infection (LRTI) with bronchiolitis and pneumonia are far more common, often with superimposed bacterial infection.⁵⁹ Similarly, LRTI with pneumonia complications are also far more frequent in older individuals and, as discussed below, especially in those with comorbidities or otherwise frail, and where exacerbations of existing cardio-pulmonary disease contribute to greater adverse outcomes.^{15,21,59} In older adults with RSV, cough and dyspnea are common. Dyspnea is often severe, particularly in high-risk patients, with over 20% of cases requiring ventilatory support and admission to intensive care units (ICU).^{7,16,60} In contrast, fever is generally less frequent than found with influenza or other ILIs, occurring in less than 50% of cases, and often mild (<38°C).^{21,59,60} This aspect has implications for testing where protocols may involve overt fever as a specific testing criterion.

Immune responses to RSV are complex and, in high-risk age-groups, are influenced by either immunological immaturity (in infants) or by age-associated immune decline ‘immunosenescence’ (older individuals).⁶¹ In severe disease, tissue inflammation is mediated through T-cell (Th2) pathways and often exaggerated pro-inflammatory cytokine/chemokine responses,^{40,61} and these may also contribute to acute cardio-pulmonary exacerbations seen with RSV infection.^{16,62} RSV re-infection is common across the lifespan; in older individuals, while antibody responses against RSV infection can be robust, these are relatively short-lived, as are RSV-specific T cell responses.^{40,61}

Burden of RSV in older adults in Brazil

In Brazil, epidemiologic studies reporting on burden in older adults are relatively sparse.^{25,26} Data for RSV-SARI reported within the SIVEP-Gripe database provide a useful indication of the overall burden of severe respiratory illness due to RSV within Brazil^{29,63} (Figure 1). This database records all notified reverse transcriptase polymerase chain reaction (RT-PCR) confirmed RSV-SARI cases, where the SARI case definition involves any patient hospitalized with fever (>37.5°C), cough and sore throat, presenting with either dyspnea, oxygen

saturation <95%, respiratory distress,⁶⁴ although it should be recognized that, as we later discuss, not all SARI cases are routinely tested for RSV.

One important feature of these data is the increasing number of cases reported annually from 2013 onwards. From a temporal perspective, a general trend between 2013 and 2019 was that RSV cases in older adults aged ≥ 65 y lagged behind those in children <2 y by approximately 2 weeks. As described above, a substantial decline in RSV cases was observed in 2020, the first year of the COVID-19 pandemic. As measures to contain COVID-19 relaxed, RSV infection shows a more off-season pattern, with 2021 and 2022 each showing an initial peak in March/April followed by a second peak in the latter part of the year, from September through December (Figure 1). Such disruption to more typical patterns is not unique, with similar changes observed in both Northern and Southern temperate zones.^{51,52,55} Perhaps of greater significance is the evidence of RSV resurgence since 2020. In part, this reflects an increase in surveillance activities and testing for a wider range of respiratory pathogens, particularly from 2020 onwards to monitor COVID-19, and also changes to surveillance guidelines (with the expansion of SARI definitions to include cases without fever, especially in the elderly),^{65,66} and greater adherence to SARI notification by health practitioners across the country. While this substantial increase in recent years highlights the importance of SARIs due to RSV, it complicates making direct comparisons of disease burden in these different periods. However, looking more specifically at these recent data does allow a fuller understanding of the present burden of RSV in Brazil, which is the focus of this article.

From January 2020 to December 2022, a total of 30,934 cases of RSV-SARI were reported to the SIVEP-Gripe database. In 2020, 1,681 cases were reported, peaking in March, after which a relatively low number of cases were reported for this year (when stringent COVID-19 mitigation strategies were in place). This was followed by RSV resurgence, and some disruption to typical seasonal patterns. In 2021, 12,478 cases were reported, with an initial peak in mid-March, followed by a gradual decline and then increasing case numbers, with a second peak in November maintained until the year-end. In

2022, 16,775 cases were reported, with a marked increase in cases from February onwards, peaking in April and then with a marked decline followed by a further increase in RSV-SARI case numbers, and then with a marked decline followed by a further increase in RSV-SARI case numbers, then subsequently increased from September onwards. This two-peak pattern was not observed in Brazil before COVID-19 introduction in 2020 and is a clear signature of the disruption of RSV-SARI seasonality in the country. Whether this scenario will be the new seasonal pattern or just a transition phase before re-establishing a stable one-peak season remains to be seen. It should be noted that most cases were reported in young children <5 y of age. However, in 2022, 934 RSV-SARI cases were reported in those aged ≥ 60 y (Figure 2 and Supplementary Table S1). More detailed temporal data from the SIVEP-Gripe database which may inform RSV transmission patterns between different age groups are currently being evaluated. A high proportion of these hospitalized older adults required ICU admission (approaching

30% in each of these years, Supplementary Table S2). RSV-SARI associated mortality was also substantial, especially in older adults (Figure 3). Between 2020 and 2022 a total of 852 deaths due to RSV-SARIs were reported in the SIVEP-Gripe database. While RSV-SARIs in those aged ≥ 60 y accounted for 5.7% of all such cases across this period, deaths in older adults accounted for 48% of all notified RSV-SARI deaths. Fatality rates were far more significant in those aged ≥ 60 y, with a case fatality rate (CFR) of 32.4% for hospitalized RSV-SARI cases in 2020 and 20.8% in 2022 (Figure 3). In contrast, CFRs for those aged ≤ 9 y were between 1–2%, a feature also reported in other studies evaluating pediatric RSV-SARI over this same period.^{31,67} Another recently reported study, evaluating RSV-confirmed ARI and hospitalized SARIs in the southeast of Brazil (Rio Grande do Sul) in 2021, also reported high fatality for RSV-SARI in hospitalized patients aged ≥ 60 y (31.2%), and where 73.6% of all deaths in patients hospitalized with RSV were in this older population.³¹

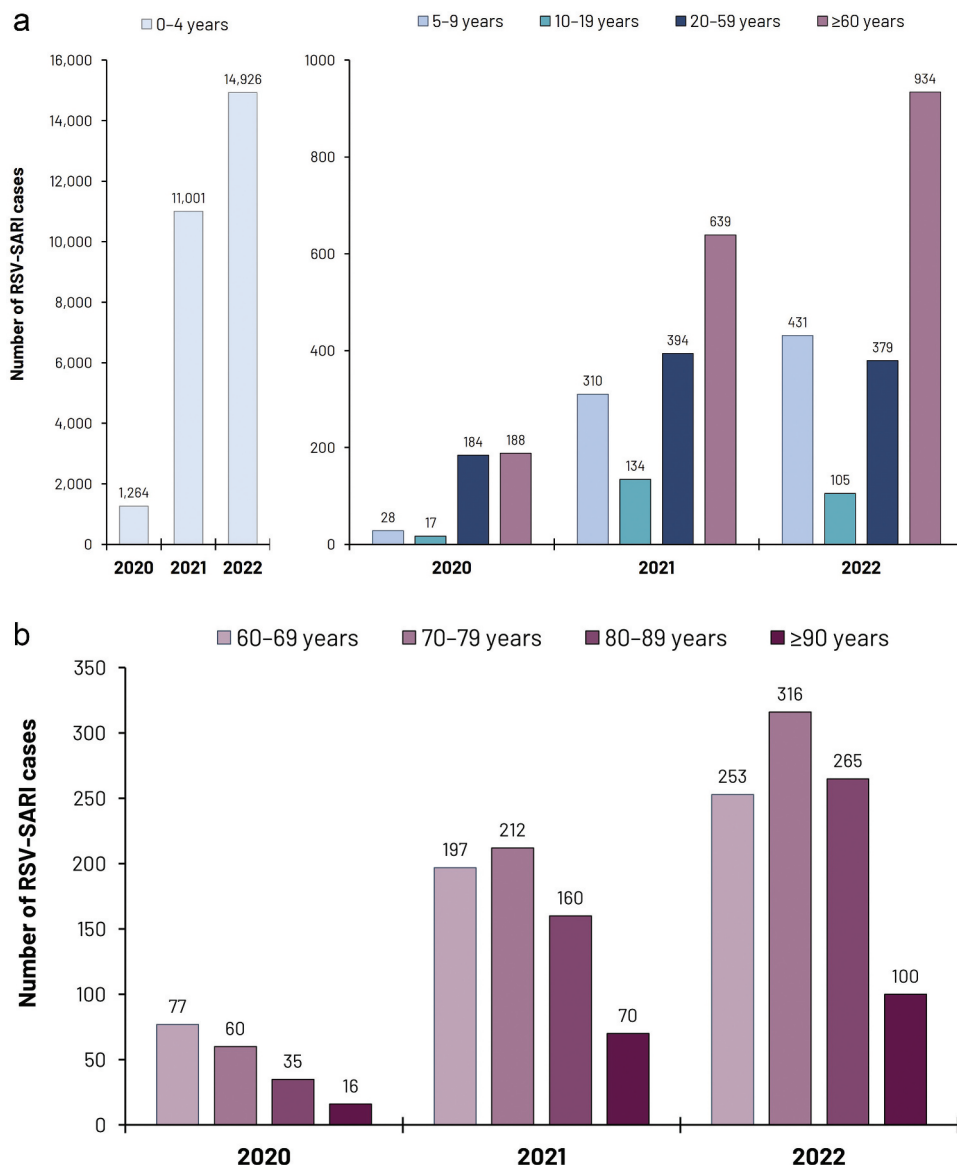


Figure 2. RSV-SARI case numbers reported within the SIVEP-Gripe database 2020–2022. Upper panel (a) reports the number of reported RSV-SARI cases in different age strata. Lower panel (b) reports RSV-SARI cases in specific age-strata in older adults. Abbreviations: RSV; respiratory syncytial virus; SARI: severe acute respiratory infection

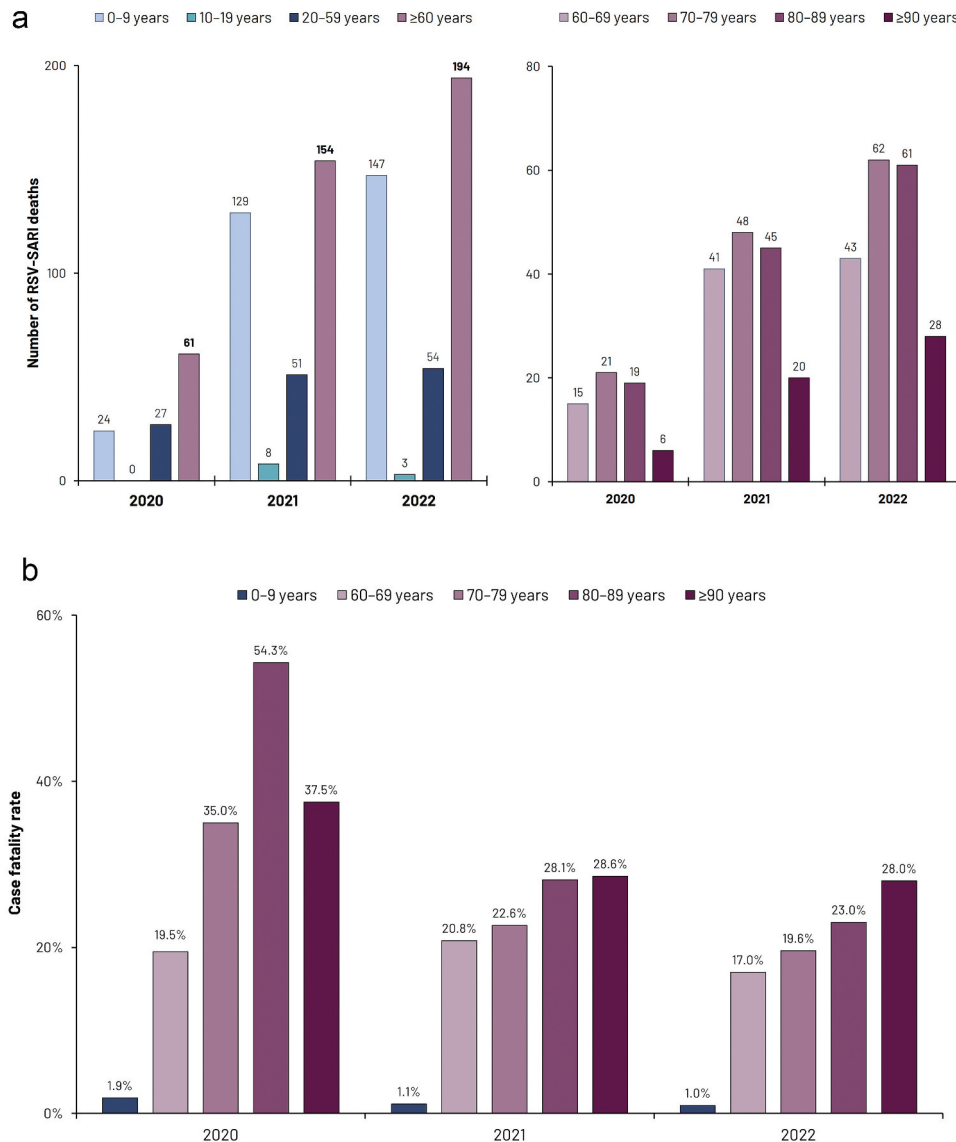


Figure 3. RSV-SARI mortality 2020–2022. Upper panel (a) reports the number of reported RSV-SARI deaths in different age strata. Lower panel (b) illustrates case fatality rates. Abbreviations: RSV; respiratory syncytial virus; SARI: severe acute respiratory infection

These high fatality rates in older adults are similar to, if not greater than those reported for influenza SARI cases, with one recent study also utilizing SIVEP-Gripe data reporting CFRs of between 19–22% in those aged 60–79 y,⁶⁸ while another reported a CFR of 24.6%.⁶⁹ Based on population demographics,⁷⁰ overall mortality rates in those aged 60–69 y across 2020–2022 ranged from 0.09 per 100,000 in 2021 to 0.24 per 100,000 (in 2021 and 2022), with greater rates seen with increasing age; up to 2.3 per 100,000 in those aged ≥90 y in 2021 and 3.1 per 100,000 in 2022 (Supplementary Table S3).

It is worth noting that these data relate to RSV-SARI notifications and chiefly represent short-term in-hospital mortality. It is generally recognized that hospital mortality alone underestimates RSV mortality, accounting for only 25% of the overall RSV mortality in younger infants, with as much as three times as many deaths occurring within the community setting.² One might expect similar underestimations for older adult mortality due to RSV. In addition, subsequent re-hospitalization and mid- to longer-term mortality associated

with RSV in the elderly is well-recognized,¹⁶ although at present such data are lacking for Brazil.

While the data we describe here relate to SARIs within SIVEP-Gripe, such data provide only a snapshot of the overall RSV burden within Brazil, and at a national level. Other data from SIVEP-Gripe and additional reporting systems, such as that from the Instituto Todos pela Saúde (ITpS) indicate that the greatest RSV burden is observed in the South and Southeast of the country.⁴⁸ However, more data are required to fully understand regional differences in adult RSV disease in Brazil. It should also be understood that the number of cases of less severe disease within both the hospital and broader community setting (primary care and emergency department visits) will be far greater still; ITpS data, which also accounts for samples taken from outpatient care clinics, points toward this.⁷¹ A fuller analysis of such data can provide greater insights into the broader overall burden of RSV disease and the impact of healthcare resource use, which may be under considerable stress during peak seasonal months.

RSV impact on patients with comorbidities

There is a wealth of evidence that comorbidities are associated with greater adverse outcomes and poorer prognosis with RSV infection.^{4,7,11,15,16,72–79} Although risk and that associated with specific comorbidities vary across studies, most common comorbidities frequently occurring in older adults confer a substantially greater risk of RSV-related hospital admission (3–10-fold higher), more severe disease, and higher short- and long-term RSV-associated mortality.^{7,15,16} A recent large surveillance study from the US reporting on older patients hospitalized with RSV found that 95% had at least one comorbidity, most commonly obesity (37.8%), chronic obstructive pulmonary disease (COPD, 33.7%), congestive heart failure (CHF, 33.2%), diabetes mellitus (32.6%) and chronic kidney disease (29.3%).⁸⁰ Another study found that overall, older adults with any comorbidity were six times more likely to be hospitalized with RSV than otherwise healthy older individuals.^{4,15} The risk of hospitalization due to RSV disease in patients with specific comorbidities shows some variation (Figure 4). In their pooled analysis of US data (chiefly that reported by Branche et al.⁷³), McLaughlin et al. reported that COPD was associated with the greatest risk of RSV hospitalization (an almost 9-fold higher risk in those aged ≥ 65 y, and 6-fold in those aged 50–64 y).¹⁵ Substantially greater RSV hospitalization rates in adults aged ≥ 65 y were also reported for those with CHF (7-fold), diabetes (almost 5-fold), coronary artery disease (CAD, almost 5-fold), and asthma (2.4 fold).^{15,73} Greater risk was also associated with obesity.^{15,73} Other US studies also indicate higher RSV hospitalization rates in older patients with chronic kidney disease and immunocompromised older adults (including patients with solid or hematologic cancers and with HIV infection).¹⁸ These patterns are evident across most regions and different ethnic populations,^{4,7,11,15,16,72–79,81} with one systematic review reporting that one-third of high-risk

older adults with RSV infection will require hospitalization, with over 25% requiring ICU admission.⁷ While our focus here is on those older than 60 y, individuals aged ≥ 50 y with comorbidity are also at greater risk of hospitalization due to RSV infection compared to otherwise healthy individuals (Figure 4).^{15,73}

RSV-associated pneumonia complications are more common in such high-risk older adults,^{7,16} and acute exacerbations of underlying cardiopulmonary disease (COPD, acute decompensation in CHF), contribute to greater mortality in this population.^{16,62} Some studies suggest higher viral loads in adults with more severe disease, although this is an inconsistent finding.^{82,83} While estimates vary, a systematic review of studies from industrialized and also developing countries reported a CFR in older adults with a comorbidity of 11%.¹⁷ These all point toward a substantial impact of comorbidity on outcomes following RSV infection, and we should note that while our focus here is on older adults, the patterns we describe are also apparent in younger adults with comorbidity).⁷ Furthermore, older adults hospitalized with RSV show an often prolonged functional decline, with a substantial impact on routine activities.^{9,84}

Data for comorbidity status and impact in Brazilian patients with RSV are more limited, although one might expect a similar range of comorbidities to be equally prevalent, and some data indicate that adults with chronic heart are at risk of complications associated with RSV infection.⁸⁵ This assumption is supported by one recent smaller study from Sao Paulo, reporting on RSV and influenza hospitalizations in older patients (mean age 59 y) in early 2022, with most due to RSV.⁶⁰ This study reported comorbidities in 80%, including CHF (29%), diabetes (27%), COPD (10%) and renal disease (12%). In addition, high rates of ventilatory support (46%) and ICU admission (10%) were required, with a mortality of 33%.⁶⁰

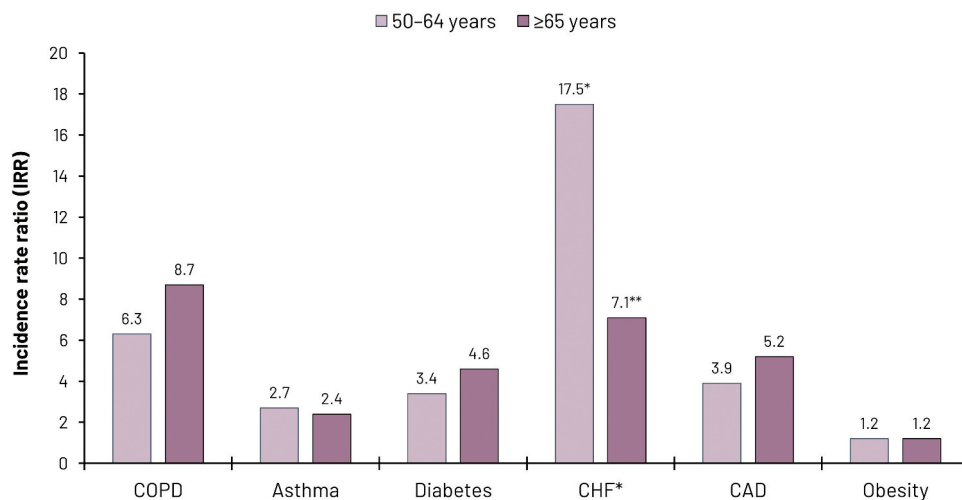


Figure 4. Risk of hospitalization due to RSV associated with comorbidities. Hospitalization risk derived from incidence rates for hospitalization in patients with and without selected comorbidities and associated incidence rate ratios. Data represents pooled analysis of data for US adults reported by McLaughlin et al.,¹⁵ derived from data originally reported by Branche et al.⁷³ * For patients with CHF, data represents individuals aged 40–59 y* and 60–79 y**. Abbreviations: CAD: coronary artery disease; CHF: congestive heart failure; COPD: chronic obstructive pulmonary disease; RSV: respiratory syncytial virus; SARI: severe acute respiratory infection; US: United States.

Perception of RSV risk in older adults and diagnostic gaps

The panel reflected on physicians' general awareness of RSV as an important pathogen in older adults, which, on balance, may be relatively low. This is not necessarily unique to Brazil; this is also generally apparent in the wider Latin American region,²⁷ and indeed in most developed countries.^{21–23} Many reasons may account for this, including a greater focus on reporting on younger children in RSV surveillance activities which could be understood to highlight RSV as solely a pediatric concern.^{3,42,48} As mentioned earlier, in the clinical setting, greater attention is paid toward influenza or SARS-CoV-2 infection as a cause of SARI in older adults, and RSV is infrequently considered. A lack of specific antiviral treatment for adult RSV infection may also contribute to RSV under testing.^{22,23} However, RSV confirmation may help identify patients at greater risk of adverse outcomes, including clinical deterioration associated with acute CHF and COPD exacerbations.^{16,62} Consequently, routine RSV testing of older adults presenting with respiratory symptoms is generally low, both in Brazil and indeed in most countries, e.g., even in hospitalized SARI cases in countries such as the US, and this represents the major limitation in establishing reliable rates for the overall RSV burden in the older population.^{20,24,86}

In Brazil, specific testing policies and processes vary across institutions, and there remains a need to establish a more uniform approach. The panels' view is that all adults presenting with acute respiratory symptoms with chronic cardiopulmonary comorbidities (e.g., CHF, CAD, COPD, asthma, uncontrolled hypertension), and those with diabetes or chronic renal disease should be tested for RSV, as should immunocompromised patients. In addition, patients presenting with acute comorbidity exacerbations (e.g., acute cardiac decompensation) should be questioned about recent respiratory symptoms, and RSV should be considered as a contributory factor. To this point, we would note that while historically, SARI case definitions have included fever as a key criterion, fever is often absent or mild in older patients with RSV, and while fever is important, the current guidance does not require fever as a core criterion for considering RSV infection or indeed any ILI.⁶⁵ More broadly, we would advocate for greater routine RSV testing for all adults aged ≥ 60 y with respiratory symptoms, in particular, those within long-term care facilities or other institutional settings where acute ILI outbreaks are well recognized.⁸⁷ While our focus is on adults aged ≥ 60 y, we would also advocate for routine RSV testing of younger adults, with comorbidities presenting with ILI-symptoms.

A wide range of antigenic and molecular tests can be used in the clinical setting, with results obtained directly at the point-of-care or following laboratory analysis.^{88–90} While testing is usually performed on specimens from nasal/nasopharyngeal swabs, aspirates or nasal wash specimens may yield greater sensitivity. Using sputum samples improves RSV detection and can be especially useful in older adults with more severe LRTI.^{15,86,91} Antigenic tests such as rapid antigen detection tests (RADTs), direct or indirect immunofluorescence (IF), and molecular methods, i.e., RT-PCR assays, each have

a place in routine diagnosis, although with differing sensitivity, specificity and costs. Molecular RT-PCR methods have greater sensitivity and specificity and generally are considered the gold standard in routine diagnosis,^{90,92} with multiplex assays, e.g., quadruplex assay (for influenza A and B, SARS-CoV-2, and RSV detection) particularly useful for broader initial diagnosis, although these are more expensive, an important consideration in resource-poor settings.

While RADTs and immunofluorescence assays can provide rapid results and are especially useful in younger children,^{93,94} sensitivity is far lower in older individuals, where molecular RT-PCR tests are preferred.^{90,93} This said, RADTs are an important tool, especially at initial presentation, and can also contribute to surveillance activities by providing some approximation of circulating RSV within the older adult population.²⁷

As such, although preferred and far more useful for older adults with RSV infection, routine RT-PCR use is low, partly due to associated costs, with antigenic testing being more frequently used, although far from routine. To this point, it must be recognized that test costs are relatively small when considering the overall costs of managing severe RSV disease. These aspects pose challenges to improving RSV testing and diagnosis in Brazil, and they may also differ between public and private health-care domains. Observations from the panel were that while RT-PCR testing is often covered through private insurance plans, routine molecular testing within private hospitals remains low, even in hospitalized patients, where antigenic tests may be more frequently used. In the public health-care setting, RSV diagnostic costs may contribute to the broader view (described earlier) that the diagnosis would not influence clinical care and so is unnecessary. Patient pathways may also influence diagnostic patterns. For many with acute respiratory symptoms, initial consultation will be within primary care, where routine RSV testing is generally unavailable, and if available, chiefly RADTs. There remains a need to develop and more widely deploy affordable diagnostic tests that are more suited to improve RSV diagnosis in older adults. In turn, this could also provide greater and more reliable estimates of the overall burden within Brazil.

Challenges in communicating RSV disease

The panel unanimously agreed that epidemiological data and their reporting mainly influence disease awareness and perception of RSV risk. In this respect, our data highlights RSV burden and its importance as an often-significant pathogen in older adults. However, this is just a start. There is, in fact, a wealth unpublished RSV data captured within reporting systems whether that be surveillance registries (SIVEP-Gripe, ITpS and others) or collected locally within hospitals. While such data are often available through periodic epidemiologic reports, these generally cover a range of respiratory pathogens.⁷¹ More focused analysis and formal publication of RSV disease burden and impact on health-care resources in medical journals are necessary to bring this to the attention of the wider medical community, particularly the impact of comorbidities on RSV disease outcomes in older adults. In turn, this

can improve clinical suspicion and RSV testing. To date, most reports on RSV within Brazil are generally reported in journals with an infectious disease or epidemiologic perspective. Ideally, such articles should be readily available to the broad range of specialists involved in older adult care, and also toward a primary care audience. As such, publication in specialty journals is encouraged.

Awareness of RSV in older adults within the general public in Brazil is also low, although again, this is not unique, with low awareness reported among the US public and elsewhere.^{95,96} There is a clear need for focused educational activities and disease awareness campaigns tailored toward both health-care professionals and to the lay public. Some insight into this can be gained from previous campaigns to increase awareness of other adult vaccine-preventable disease; obviously, education was a critical element of physician training during the COVID-19 pandemic.⁹⁷

While the focus of this article relates to the burden and impact of RSV-infection, effective RSV vaccines for use in adults ≥ 60 y are now available. Two such vaccines, an adjuvanted RSVPreF3 vaccine (AREXVY, GSK) and the RSVpreF vaccine (*Abrysvo*, Pfizer), each targeting the F fusion protein, have demonstrated high efficacy against RSV infection, including severe LRTI disease.^{33–35} Inclusion of an adjuvant within AREXVY enhances antibody and T-cell responses to help overcome age-related immune decline, with sustained efficacy in older adults, including those with underlying cardiorespiratory comorbidity.^{98,99} Additional vaccines are in the later stages of clinical development and regulatory approval.¹⁰⁰ Both AREXVY and *Abrysvo* are already included in national immunization recommendations for older adults in several countries, including the US,³³ where the estimated public health impact due to disease reduction in older adults is substantial.¹⁰¹ Notably, such benefits are not only for RSV-SARI; reductions in milder RSV cases requiring medical attention within primary care will far exceed RSV-SARI case numbers.¹⁰¹ In addition, specialist societies and expert initiatives such as the Global Initiative for Chronic Obstructive Disease (GOLD) and the Global Initiative for Asthma (GINA) also now recommend RSV vaccination for those aged ≥ 60 y with chronic heart or lung disease.^{102,103} In Brazil, both vaccines have now been approved (AREXVY in December 2023, and *Abrysvo* in March 2024) and available for use in adults aged ≥ 60 y, given as a single dose.^{36,37} One useful pragmatic aspect is the ability to co-administer either of these RSV vaccines along with the seasonal influenza vaccine. The Brazilian Society of Immunization (SBIm) recommends the use of RSV vaccination in all adults aged ≥ 60 y, with these endorsed by the Brazilian Society of Geriatrics and Gerontology, the Brazilian Thoracic Association (SBPT), the Brazilian Society of Cardiology and other specialist societies.^{104–108} Although their introduction is only at an early stage in Brazil and, at present, would be funded privately, RSV vaccines now provide an important tool in reducing RSV disease and resultant morbidity and mortality in older adults. Education on vaccine benefits (especially in high-risk older adults) can complement broader RSV awareness campaigns.

Conclusions

The significance of RSV as an important respiratory pathogen in older adults ≥ 60 y is generally under-recognized. Although there remains a need to better characterize the RSV burden within and across Brazil, available data indicates that RSV represents an important cause of SARI in older adults, with high impact (up to 50% of all RSV deaths in Brazil in recent years). The prognosis is poorest in patients with comorbidities. Furthermore, in part due to increased surveillance of respiratory pathogens in recent years, SARI case numbers are increasing, and although data are lacking, one may expect a similar pattern and with even greater numbers of less severe RSV cases requiring medical care. These patterns are broadly similar to those observed in other countries with more established data on the clinical burden of disease in older adults. Rates of RSV testing in the clinical setting are low, and this obscures diagnosis and hinders clinical epidemiology and broader RSV surveillance. While we provide some insight into the RSV burden, there are substantial knowledge/research gaps for Brazil, and we encourage greater data reporting and communication. Crucially, we advocate for improved testing while recognizing challenges facing clinicians and institutions in this respect. Educational initiatives and awareness campaigns will be important to improve understanding of the clinical significance of RSV in older adults. The recent availability of protective RSV vaccines offers a valuable tool for RSV prevention in this vulnerable older adult population.

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

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Author contributions

All authors were involved in the analysis and interpretation of the relevant literature and the development of the manuscript. All authors gave final approval before submission.

Data availability statement

All data generated or analyzed are included in this published article or in the original cited data sources.

Prior presentation

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Trademarks

AREXVY is a trademark owned by or licensed to GSK.
Abrysvo is a trademark of Pfizer.

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