Castro *et al. BMC Public Health* (2025) 25:3168
https://doi.org/10.1186/s12889-025-24264-0

BMC Public Health

RESEARCH Open Access

Asthma and severe acute respiratory infections: a stratified analysis of mortality patterns in Brazil

Cecilia Castro[1*], Victor Leiva[2*], Viviana Giampaoli[3], Diana Prieto[2], Carlos Martin-Barreiro[4*] and Johanna Viana[5]

Abstract

Purpose Asthma is a prevalent chronic respiratory condition. However, evidence on its association with mortality from severe acute respiratory infections (SARI), including COVID-19, remains scarce in South America, particularly in Brazil. Given asthma's potential to influence respiratory outcomes, we investigated how age and other demographic or clinical predictor variables are associated with mortality in this context.

Methods We analyzed SARI mortality data from 415,711 patients recorded in the Brazilian Unified Health System between January and December 2022. Patients were stratified by key predictors such as asthma status, age group, intensive care unit admission, and sex. Both frequentist and Bayesian logistic regression models were fitted to explore interactions among these predictors. To address class imbalance (fewer deaths relative to recoveries), we applied data-balancing techniques before model estimation.

Results Older age and admission to an intensive care unit were strong predictors of death. Invasive mechanical ventilation emerged as the single strongest clinical marker of severity, with an adjusted odds ratio (OR) of approximately 14.7, though this was exceeded by the effect of age, whose influence on mortality was even greater. Asthma was associated with lower mortality overall (adjusted OR ≈ 0.31), although the protective association weakened in young adults aged 19–29 years (OR ≈ 0.69) and in adults aged ≥ 79 years (OR ≈ 0.72). Vaccination against COVID-19 or influenza, as well as the use of antivirals, were each linked to lower mortality. The final model showed good discrimination, with an area under the receiver operating characteristic curve of 0.845.

Conclusion Asthma is associated with lower odds of death, but the strength of this protective association diminishes in early adulthood and again in later life. These age-related differences warrant further investigation and, if confirmed, could inform age-tailored care strategies. Maintaining broad vaccine coverage and timely antiviral use remains advisable for all patients. Future studies that incorporate detailed information on asthma control, medication adherence and lifestyle factors are needed to clarify the mechanisms underlying these patterns.

Keywords Bayesian analysis, COVID-19 mortality, Logistic regression, Public health, Respiratory diseases

*Correspondence:
Cecilia Castro
cecilia@math.uminho.pt
Victor Leiva
victorleivasanchez@gmail.com; victor.leiva@pucv.cl
Carlos Martin-Barreiro
cmmartin@espol.edu.ec

Full list of author information is available at the end of the article

Introduction

Asthma is a complex and heterogeneous chronic respiratory disease that affects millions of people worldwide [1], contributing to high morbidity, premature mortality, and, in occupationally exposed groups, reduced work productivity [2]. It is characterized by chest tightness, coughing, shortness of breath, and wheezing, often accompanied by expiratory airflow limitation [3]. The disease requires individualized assessment and can markedly impair quality of life [3]. Although the global burden remains high, recent estimates indicate a rising prevalence among children and adolescents [4]. This highlights the importance of coordinated international initiatives such as the Global Asthma Network and the International Study of Asthma and Allergies in Childhood program, which have enhanced global data collection and supported evidence-based management strategies [5].

Advances in artificial intelligence, data science, machine learning, and distributed ledger technologies have accelerated asthma research. Recent developments include machine-learning-based prediction of pediatric asthma exacerbations [6], deep learning for adult diagnosis [7], and risk score models for childhood-onset asthma [8], alongside artificial intelligence applications originally designed for other chronic or infectious diseases [9–11]. A bibliometric analysis further confirms the rapid growth of blockchain applications in clinical research and data governance [12].

AI-assisted clinical decision support, particularly in pediatric care, holds promise for optimizing treatment and reducing exacerbations [13–15]. The integration of electronic health record data enables phenotype identification and early detection of high-risk patients, thereby fostering proactive care [16–19]. More broadly, artificial intelligence and machine learning contribute to precision healthcare by supporting patient-specific interventions in respiratory medicine [20–23], and have also been applied to develop diagnostic and prognostic tools for COVID-19 [24, 25].

Wearable technology and big data analytics are transforming the management of chronic conditions by enabling continuous data capture and real-time monitoring [6, 26]. When combined with interpretable machine learning frameworks, these data streams support early diagnosis and identification of high-risk subgroups, thereby enhancing resource allocation in public health systems [9–11].

Despite these technological advances, the emergence of severe acute respiratory infections (SARI), including COVID-19, has raised important questions about how asthma influences respiratory outcomes. Descriptive studies suggest that asthma may not universally increase SARI mortality [27, 28], whereas cohort studies show that outcomes vary depending on asthma control, pharmacotherapy, and vaccination status [29, 30]. Comorbidities, demographic factors or predictor variables (hereafter "predictors"), and micronutrient status—such as vitamin D metabolites—also affect SARI outcomes among individuals with asthma [31–33]. Vaccination appears to confer a protective effect in mitigating infection severity among patients with asthma or chronic obstructive pulmonary disease [34], although intensive care unit (ICU)-based studies report heterogeneous outcomes across different phases of the COVID-19 pandemic [35]. The multifactorial nature of these determinants underscores the complexity of SARI risk in asthmatic populations.

Large-scale surveillance data from the Brazilian Ministry of Health [36], together with global datasets, support the application of robust analytical methods. Bayesian approaches allow formal quantification of uncertainty in model parameters [37, 38], while specialized resampling techniques address the class imbalance often present in SARI data [39, 40]. Recent studies have also focused on improving model interpretability through local and Shapley value-based explanation methods [41–43], although these techniques have yet to be systematically applied to SARI risk prediction. Moreover, meta-analyses often combine data from regions with healthcare systems that differ substantially from those in South America [27], and even studies that include Latin America frequently fail to account for regional specificities that influence clinical outcomes [28, 44]. As a result, a comprehensive evaluation of the relationship between asthma and SARI mortality in South America is still lacking.

To address this gap, we analyzed data from 415,711 hospitalized patients recorded in Brazil's Unified Health System between January and December 2022 [36]. We examined the association between asthma and SARI mortality, including COVID-19, while adjusting for age, sex, comorbidities, and vaccination status. Risk estimates were refined using frequentist and Bayesian logistic regression models, with class imbalance mitigated through the synthetic minority over-sampling technique (SMOTE)-based resampling methods [39, 40] in a coherent probabilistic framework [37, 38]. Our findings aim to inform targeted public health interventions for patients with asthma hospitalized with SARI in the Brazilian context.

The article is organized as follows. "Materials and methods" section describes the data sources, variable definitions, and logistic regression methods. In "Results" section, we present the results, including logistic regression analyses. In "Discussion" section, clinical implications, study limitations, and directions for future research are discussed. "Conclusions" section concludes by outlining the main contributions and potential applications of our findings in public health.

Materials and methods

This section describes the dataset, key variable definitions, and the methodological framework, including logistic regression modeling and data-balancing techniques.

Dataset and source

This study uses data from the official surveillance system for SARI maintained by the Brazilian Ministry of Health. The surveillance network, known as SIVEP-Gripe (Sistema de Informação de Vigilância Epidemiológica da Gripe, in Portuguese, the national epidemiological surveillance system for influenza and other respiratory viruses), was initially established to monitor influenza A(H1N1)pdm09 in 2009 and was expanded in 2020 to include COVID-19 surveillance. The SIVEP-Gripe database is part of DATASUS (Departamento de Informática do Sistema Único de Saúde —SUS—, in Portuguese), the Brazilian public healthcare information system, which integrates data reported by both public and private hospitals, including those regulated by the ANS (Agência Nacional de Saúde Suplementar, in Portuguese), the Brazilian regulatory agency for private healthcare. Reporting of SARI cases is mandatory for all healthcare facilities, ensuring comprehensive epidemiological surveillance.

We describe the data access and anonymization, study population and data source, as well as the inclusion of private healthcare data as follows:

- Data access and anonymization —The dataset used here is publicly available and anonymized in accordance with the Brazilian General Data Protection Law (Lei n. 13.709/2018). To reproduce this study, readers can access the data through the Brazilian Ministry of Health's open data webpage [36]. On this webpage, users should navigate to the section titled Recursos (Resources), select the relevant year (for this analysis, 2022), and download the desired file format (such as comma-separated values —CSV— files, *.csv). Each file includes nationwide reports of SARI cases (including COVID-19) reported from all Brazilian states and municipalities. Because updates and corrections are periodically implemented by local and regional epidemiological teams, exact record counts may vary slightly depending on the download date.
- Inclusion of private healthcare data —The SIVEP-Gripe database integrates notifications from both public hospitals affiliated with the Brazilian Unified Health System and private hospitals regulated by the National Supplementary Health Agency (ANS). As of December 2024, approximately 24.5% of the Brazilian population was covered by private health plans (an increase from 23.2% in December 2022), with regional variations reaching nearly 50% in certain southeastern states, such as São Paulo and Rio de Janeiro [45]. All healthcare facilities, both public and private, are legally mandated to report SARI cases to the SIVEP-Gripe system [36]. This comprehensive reporting ensures that the dataset used in our study encompasses a broad spectrum of the Brazilian healthcare system, helping to mitigate potential biases arising from sectoral differences.
- Study population and data source —We included all anonymized SARI notifications reported between January and December 2022 from the SIVEP-Gripe database, covering the entirety of Brazil. As this study involved secondary analysis of publicly accessible, de-identified data, ethical approval was waived.

Variable definitions and data processing

From this national surveillance dataset, 14 key demographic and clinical variables relevant to SARI hospitalizations were selected. The original SIVEP-Gripe system records age numerically. However, the publicly available data provide age categorized into standardized intervals. This categorization is applied by the surveillance system during data extraction, particularly when exact birth dates are missing and age is estimated. For consistency and analytic convenience, we retained these categorical age intervals throughout our analyses.

The selected variables and their respective categories are presented as follows:

- AGE —It represents the patient age categorized into nine groups, recorded as (0,9], (9,19], (19,29], (29,39], (39,49], (49,59], (59,69], (69,79], and (79,+infinite) years old.
- ANTIVIRAL —It indicates if the patient used antiviral drugs for the flu, recorded as Yes/No.
- ASTHMA —It states if the patient has asthma, recorded as Yes/No.
- CARDIO —It establishes the presence of cardiovascular disease, recorded as Yes/No.
- CFCLASS —It is the classification of SARI subtype defined by specific etiologies, including COVID-19-related SARI, influenza-related SARI, unspecified SARI, SARI due to other etiologic agents, and SARI associated with other respiratory viruses.
- COVVAC —It is the COVID-19 vaccination status, recorded as Yes (vaccinated) or No (not vaccinated).
- DYSPNEA —It indicates if the patient experiences shortness of breath, recorded as Yes/No.
- EVOLUT —It corresponds to the patient outcome, categorized as Recovered/Died.
- FLUVAC —It represents the influenza vaccination status, recorded as Yes/No.
- ICU —It indicates whether the patient was admitted to the ICU, recorded as Yes/No.

- OXYGEN —It is the type of oxygen support received, categorized as No (no support), Yes_non_invasive (non-invasive support), or Yes_invasive (invasive support).
- RESPDIS —It indicates if the patient suffers from respiratory distress, recorded as Yes/No.
- SATUR —It is an indicator of oxygen saturation (O_2) issues, recorded as Yes/No.
- SEX —It is the biological sex assigned at birth, recorded as Female/Male.

Analytical methods

A descriptive analysis was conducted to compare clinical and demographic characteristics by asthma status, using frequencies, percentages, and chi-square (χ^2) p-values to assess statistical significance between asthmatic and non-asthmatic groups. Based on these preliminary assessments and clinical plausibility, several candidate interactions were identified for consideration in our logistic regression models, including the following:

- Asthma × Age —Given distinct mortality patterns across age groups among asthmatics.
- Asthma × ICU Admission —To explore how critical care might differentially affect asthmatics.
- Age × ICU Admission —Motivated by the possibility that ICU care could have heterogeneous effects by age.
- Sex × Age and Sex × ICU Admission —Given indications of sex-specific responses in critical care outcomes and varied mortality patterns in different age brackets.

To quantify the effects of key predictors and their potential interactions, we applied both frequentist and Bayesian logistic regression models [15, 38]. By integrating prior information, the Bayesian approach generated posterior distributions for each coefficient, allowing for probabilistic interpretations through credible intervals (CrI) that complemented frequentist confidence intervals. For example, a 95% CrI indicates a 95% probability that the true parameter lies within the interval, given the data and priors. This perspective enhances the interpretability of predictor effects and interactions.

Model-building procedure

All candidate interactions were initially included in both models. Subsequently, the following procedures were applied:

- Backward elimination (frequentist) —Interactions that did not meet a predefined statistical significance threshold ($\alpha = 0.05$) were removed unless there was a compelling clinical rationale for retaining them.
- Posterior distributions (Bayesian) —For each interaction, we examined whether the 95% CrI excluded the null (OR = 1). Interactions with wide CrI centered near one were considered uninformative unless supported by strong clinical justification.
- Clinical plausibility and parsimony —Interactions supported by prior research or deemed biologically meaningful were considered for retention, provided they did not overly complicate the model without improving interpretability.

Following these procedures, a final model was obtained for both the frequentist and Bayesian analyses. Details on which interactions remained are presented in "Logistic regression analyses" section, along with their estimated effects and implications.

Model fit and performance indicators

We evaluated the suitability of the logistic regression models using fit and performance indicators relevant to clinical and public health contexts. These indicators provide insights into model accuracy, robustness to class imbalance, and sensitivity in detecting high-risk cases [39]. The evaluated indicators include the following:

- Accuracy —It is the overall ratio of correct predictions across all instances. While it provides a general performance measure, accuracy may be less informative in imbalanced datasets where one class dominates.
- Sensitivity (recall) —It is the proportion of true positive predictions among all actual positives, reflecting the model's ability to correctly identify patients at high risk of mortality.
- Specificity —It is the proportion of true negative predictions among all actual negatives, indicating the model's ability to correctly identify patients who did not experience mortality.
- Precision —It is the proportion of true positive predictions among all positive predictions, indicating the reliability of predictions that identify high-risk patients.
- F1 score —It is the harmonic mean of precision and recall. This measure balances sensitivity and precision and is particularly valuable in imbalanced datasets.
- Receiver operating characteristic area under the curve (ROC-AUC) —It is the area under the receiver operating characteristic curve, which reflects the trade-off between sensitivity and specificity over varying thresholds. It offers a global measure of model discrimination.

- Negative predictive value —It is the proportion of true negative predictions among all predictions classified as negative, indicating how reliably the model identifies non-mortality cases.
- False positive rate —It is the proportion of false positive predictions among all actual negatives, providing insight into the rate of false alarms in mortality prediction.
- Balanced accuracy —It is the average of sensitivity and specificity, giving equal weight to both classes, and providing a more robust performance measure in the presence of class imbalance.

These indicators form a comprehensive framework for evaluating model performance, focusing on identifying high-risk cases and minimizing misclassifications. Using this range of metrics, we assess the model's ability to support clinical decision-making and public health strategies for managing SARI patients with asthma.

Data-balancing techniques

In imbalanced datasets—where one outcome class greatly outweighs the other—model performance may become biased. In our study, recovery cases greatly exceeded mortality cases, reducing the model's sensitivity to the minority class (mortality), which is crucial for assessing mortality risk factors [39, 40].

To mitigate class imbalance, we utilized the following data balancing techniques:

- Undersampling —It involves reducing the size of the majority class by randomly removing instances, thereby balancing the dataset. While undersampling can prevent the model from being biased toward the majority class, it may lead to information loss due to the reduced sample size of the majority class.
- Oversampling —It increases the representation of the minority class by duplicating existing observations or generating synthetic instances. Oversampling enhances the model's ability to learn from the minority class but can increase the risk of overfitting, as the model may learn patterns specific to duplicated instances rather than generalizable patterns.
- Hybrid methods —It includes techniques like SMOTE, which combine oversampling of the minority class with the creation of synthetic instances based on feature space similarities. This approach can improve model generalization by providing new and diverse instances without merely duplicating existing ones.

All techniques were applied, and sensitivity analyses confirmed that the choice of balancing method did not substantially affect the results.

We chose undersampling for presenting results, justified by the following:

- Computational efficiency —It reduced the computational resources required for model training, which was particularly important for running the Bayesian logistic regression models, as they are computationally intensive and memory-demanding.
- Large dataset —Given our substantial dataset, undersampling the majority class (recovery cases) still left us with a sufficient number of instances to maintain statistical power and model reliability. The reduction did not highly impact the model's ability to detect relevant patterns or associations.
- Model stability —It minimized the risk of overfitting associated with oversampling techniques. By reducing the majority class rather than increasing the minority class, we avoided introducing redundant information that could bias the model.

Results

This section presents the findings of the study, including the sensitivity analysis, exploratory data analysis, and logistic regression results.

Sensitivity analysis

Our sensitivity analysis indicated that the main predictors and their associations with SARI mortality remained consistent across different data balancing techniques, including undersampling, oversampling, and SMOTE [39, 40]. This consistency suggests that our results are stable regardless of the balancing technique used, which is likely attributable to the large size of our dataset. Full details of the sensitivity analysis are available upon request.

Exploratory analysis

Preliminary analyses explored associations between asthma, age, comorbidities, ICU admission, SARI mortality, and vaccination status by stratifying variables according to asthma status, age group, and sex. This provided initial insights into mortality patterns and respiratory health variations across clinical and demographic subgroups, guiding the development of our statistical models.

Table 1 presents the distribution of clinical and demographic characteristics by asthma status, including frequencies, percentages, and chi-square p-values to assess statistical significance between asthmatic and non-asthmatic groups.

Patients with asthma represented only 4.6% of the dataset, highlighting their limited prevalence in the cohort. However, the large sample size of 415,711 individuals enables meaningful comparisons despite the small

proportion of asthmatic cases. The age distribution shows a high concentration of younger patients in the asthmatic group, with 43.6% aged 0 to 9 compared to 25.2% among non-asthmatics; see Table 1 and Fig. 1 supporting such findings. These patterns indicate that asthmatic children represent a relatively larger share of SARI cases, which is important for understanding how outcomes vary with age in this group. Conversely, older age groups (69–79 years and 79 years or older) are less represented among asthmatics, suggesting potential differences in how asthma relates to SARI risk across life stages.

The classification of SARI types also varied between groups. A high proportion of non-asthmatic patients (46.1%) and asthmatic patients (25.8%) were classified as COVID-19-related SARI. However, 62.3% of asthmatic patients were categorized as unspecified SARI, compared to 44.6% among non-asthmatics. These differences in classification may reflect variation in diagnostic specificity or reporting practices between the groups, and point to possible challenges in characterizing the etiology of respiratory infections among patients with asthma.

Gender distribution differed between groups, with females comprising 55.5% of the asthmatic group versus 48.9% in non-asthmatics. This pattern may suggest a high asthma prevalence among female SARI patients, although this observation requires further investigation.

Clinical symptoms such as dyspnea and respiratory distress were more frequently reported among asthmatics. Dyspnea was present in 77.5% of asthmatics compared to 59.3% of non-asthmatics, while respiratory distress

Table 1 Distribution of clinical and demographic characteristics by asthma status with Brazilian data

Variable	Class/Level	No (396,530 patients, 95.4%)	Yes (19,181 patients, 4.6%)	*p*-value
AGE	(0,9]	99,874 (25.2%)	8,371 (43.6%)	< 0.001
	(9,19]	15,305 (3.9%)	1,357 (7.1%)	
	(19,29]	13,814 (3.5%)	622 (3.2%)	
	(29,39]	16,695 (4.2%)	736 (3.8%)	
	(39,49]	20,913 (5.3%)	956 (5.0%)	
	(49,59]	31,660 (8.0%)	1,221 (6.4%)	
	(59,69]	49,903 (12.6%)	1,745 (9.1%)	
	(69,79]	63,525 (16.0%)	1,933 (10.1%)	
	(79, +infinite)	84,841 (21.4%)	2,240 (11.7%)	
SEX	Female	194,061 (48.9%)	10,641 (55.5%)	< 0.001
	Male	202,469 (51.1%)	8,540 (44.5%)	
DYSPNEA	No	161,197 (40.7%)	4,313 (22.5%)	< 0.001
	Yes	235,333 (59.3%)	14,868 (77.5%)	
RESPDIS	No	202,514 (51.1%)	6,766 (35.3%)	< 0.001
	Yes	194,016 (48.9%)	12,415 (64.7%)	
SATUR	No	190,991 (48.2%)	5,997 (31.3%)	< 0.001
	Yes	205,539 (51.8%)	13,184 (68.7%)	
CARDIO	No	292,783 (73.8%)	15,247 (79.5%)	< 0.001
	Yes	103,747 (26.2%)	3,934 (20.5%)	
FLUVAC	No	362,231 (91.4%)	17,002 (88.6%)	< 0.001
	Yes	34,299 (8.6%)	2,179 (11.4%)	
ANTIVIRAL	No	380,941 (96.1%)	18,046 (94.1%)	< 0.001
	Yes	15,589 (3.9%)	1,135 (5.9%)	
ICU	No	292,543 (73.8%)	14,527 (75.7%)	< 0.001
	Yes	103,987 (26.2%)	4,654 (24.3%)	
OXYGEN	No	108,781 (27.4%)	3,975 (20.7%)	< 0.001
	Yes (invasive)	47,222 (11.9%)	1,708 (8.9%)	
	Yes (non-invasive)	240,527 (60.7%)	13,498 (70.4%)	
EVOLUT	Died	88,104 (22.2%)	1,966 (10.2%)	< 0.001
	Recovered	308,426 (77.8%)	17,215 (89.8%)	
COVVAC	No	151,880 (38.3%)	8,110 (42.3%)	< 0.001
	Yes	244,650 (61.7%)	11,071 (57.7%)	
CFCLASS	COVID-19	182,842 (46.1%)	4,955 (25.8%)	< 0.001
	Influenza	9,149 (2.3%)	737 (3.8%)	
	Not specified	176,839 (44.6%)	11,955 (62.3%)	
	Other etiologic agent	3,337 (0.8%)	156 (0.8%)	
	Other respiratory virus	24,363 (6.1%)	1,378 (7.2%)	

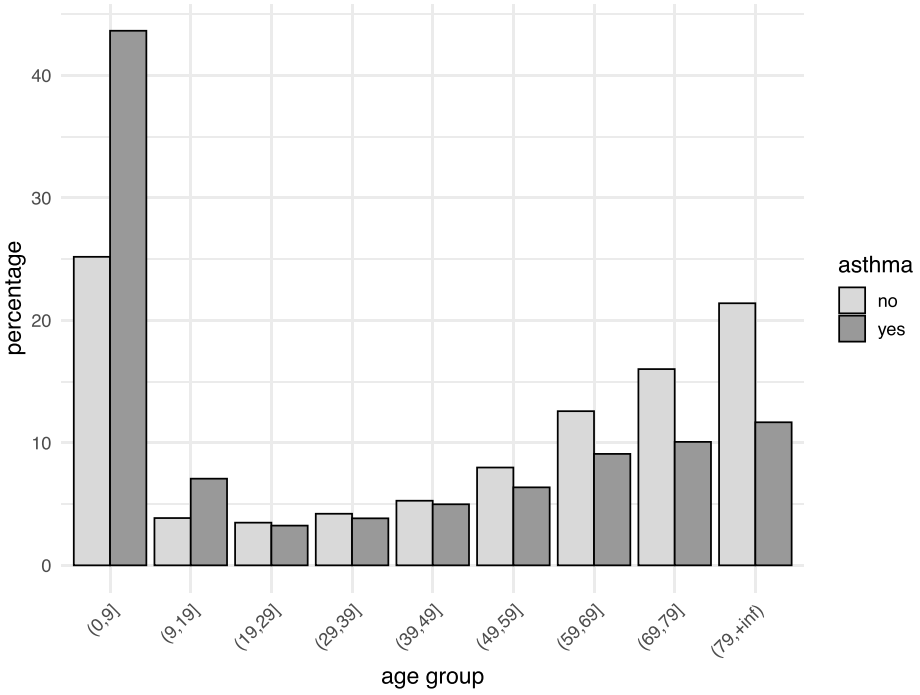

Fig. 1 Bar plot of age distribution of SARI patients by asthma status with Brazilian data

Table 2 Distribution of patient outcomes by asthma status with Brazilian data

	Percent of patients	
Asthma status	**Died**	**Recovered**
Non-asthmatic	22.2	77.8
Asthmatic	10.2	89.8

affected 64.7% and 48.9%, respectively. These findings indicate that asthma is associated with an increased frequency of respiratory symptoms, which may influence the clinical presentation and course of SARI in this population.

Vaccination rates for influenza and COVID-19 differed modestly between groups, as shown in Table 1. Influenza vaccination was more common among asthmatics (11.4%) than non-asthmatics (8.6%), possibly reflecting greater awareness or prioritization of vaccination in this subgroup. In contrast, COVID-19 vaccination rates were slightly lower among asthmatics (57.7%) compared to non-asthmatics (61.7%).

A detailed analysis of mortality rates by asthma and vaccination status is presented in Table 2. Non-asthmatic patients exhibited a mortality rate of 22.2%, much higher than the 10.2% observed among asthmatic patients (χ^2 = 1543.6, degrees of freedom = 1, p-value < 0.01). These results indicate a low observed mortality among patients with asthma. However, this should be interpreted with caution, as unmeasured confounders or differences in clinical management may underlie the observed pattern.

Table 3 Mortality by asthma status and vaccination status (absolute numbers and percentages) with Brazilian data

		Number of patients		Percent of patients	
Asthma	**Vaccination**	**Died**	**Survived**	**Died**	**Survived**
Asthmatic	Unvaccinated	364	7,746	4.5	95.5
Asthmatic	Vaccinated	1,602	9,469	14.5	85.5
Non-asthmatic	Unvaccinated	19,641	132,239	12.9	87.1
Non-asthmatic	Vaccinated	68,463	176,187	28.0	72.0

Table 3 presents the absolute number and percentage of deaths among vaccinated versus unvaccinated individuals, stratified by asthma status. Notably, non-asthmatic patients who were vaccinated exhibited a 28.0% mortality rate, compared to 12.9% among unvaccinated non-asthmatics. A similar pattern is observed among asthmatic patients: 14.5% mortality in vaccinated individuals versus 4.5% in the unvaccinated group. A chi-square test confirmed the statistical significance of these differences (χ^2 = 14,328, degrees of freedom = 3, p-value < 0.01).

Although initially counterintuitive, the high mortality rates observed among vaccinated individuals are likely influenced by confounding, particularly by age and comorbidities. Older or more clinically vulnerable patients were often prioritized for vaccination, which may partially account for these patterns. To further explore this relationship, we computed mortality rates stratified by asthma status, vaccination status, and age.

Figure 2 presents a line graph illustrating age-specific mortality rates stratified by asthma and vaccination status. The x-axis indicates the age brackets, while the y-axis represents the mortality rate (in percent). Each panel (facet) distinguishes asthmatic from non-asthmatic patients, and within each panel, the lines and points differentiate vaccinated from unvaccinated individuals.

From Fig. 2, we observe that beginning in the 19–29 age bracket, unvaccinated individuals consistently exhibit greater mortality rates than their vaccinated counterparts, both among asthmatics and non-asthmatics. This aligns with the notion that vaccination may be associated with low mortality risk, although interpretation must remain cautious due to potential residual confounding and lack of adjustment for baseline clinical severity.

Figure 3 shows a line plot of mortality rates among ICU patients segmented by age, asthma status, and sex. Non-asthmatic patients consistently exhibit high mortality percentages across all age groups. Among asthmatic males, mortality rates increase sharply between the 9–19 and 19–29 age groups, stabilize until 49 years, and then rise again, peaking at 69–79 years, with a slight decline beyond 79 years. In contrast, asthmatic females display a more gradual and steady increase in mortality with age. Among non-asthmatic males, mortality rates are particularly elevated in older age groups.

Figure 4 expands this analysis by incorporating COVID-19 status. The data indicate that, among asthmatic males, SARS-CoV-2 infection is associated with an amplified age-related rise in mortality. For instance, in the 19–29 age group, asthmatic males with COVID-19 exhibit a mortality rate more than twice that of their non-COVID counterparts, and among those aged from 49 years onward, mortality in COVID-19 cases exceeds 40%. In older age groups, non-asthmatic individuals consistently show high mortality rates overall, regardless of whether the SARI case was attributed to COVID-19 or other etiologies. These patterns suggest that COVID-19 may be linked to greater vulnerability among younger and middle-aged asthmatic men, while non-asthmatic patients continue to experience the highest absolute mortality burden at advanced ages.

Respiratory health differences were further explored by examining O_2 saturation across age groups, stratified by asthma status and sex. As noted in Table 1, 68.7% of asthmatic patients presented with low O_2 saturation, compared to 51.8% among non-asthmatics.

Figure 5 provides a stacked-bar chart showing the percentage of low (dark gray) versus normal (light gray) O_2 saturation across age brackets. A dashed horizontal line at the 50% mark aids interpretation. Among asthmatic individuals, the dark-gray segment exceeds half of each bar across nearly all age groups, indicating that more than 50% of asthmatic patients experienced low saturation. By contrast, among non-asthmatics, the proportion of low saturation exceeds 50% only in older groups (from 49 years onward), and remains consistently lower than that observed in asthmatics.

Low O_2 saturation is a well-established clinical indicator of respiratory compromise and is frequently associated with severe outcomes, including mortality. Interestingly, although patients with asthma more often presented with low O_2 saturation, our results show low observed mortality in this group. This apparent inconsistency may reflect differences in healthcare-seeking behavior, earlier clinical intervention, or unmeasured

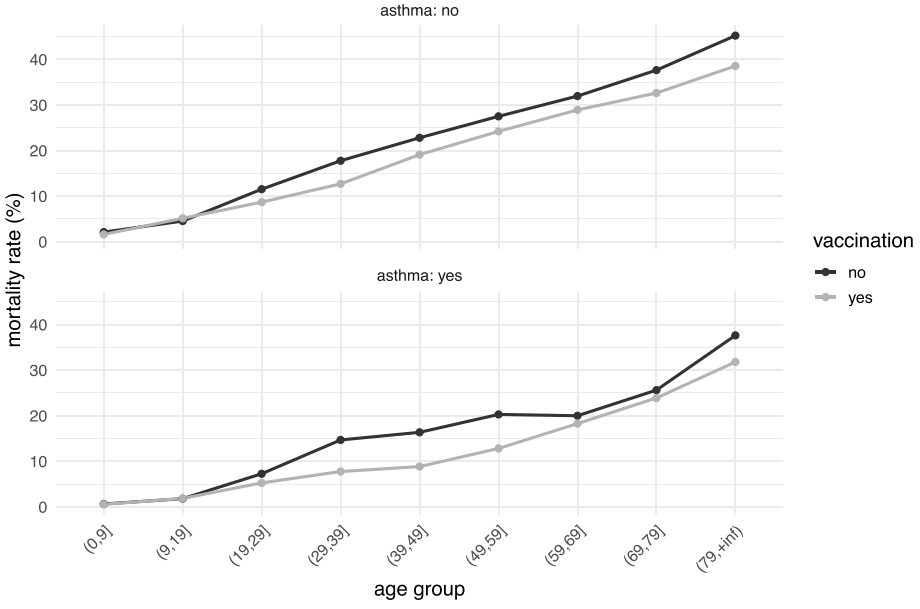

Fig. 2 Line plot comparing mortality rates by age group, asthma status, and COVID-19 vaccination status using Brazilian data

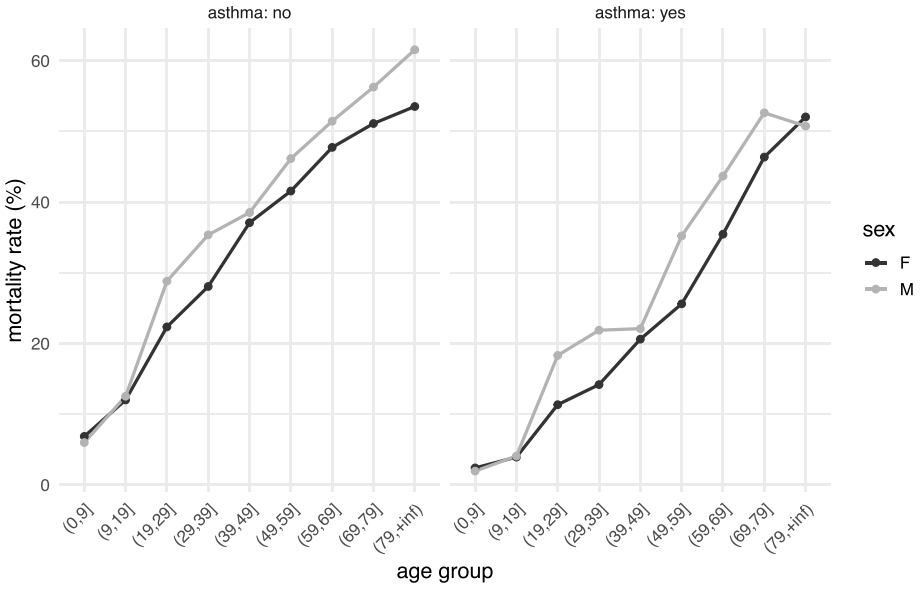

Fig. 3 Line plot of mortality rates of ICU patients by age group, asthma status, and sex —female (F)/male (M)— with Brazilian data

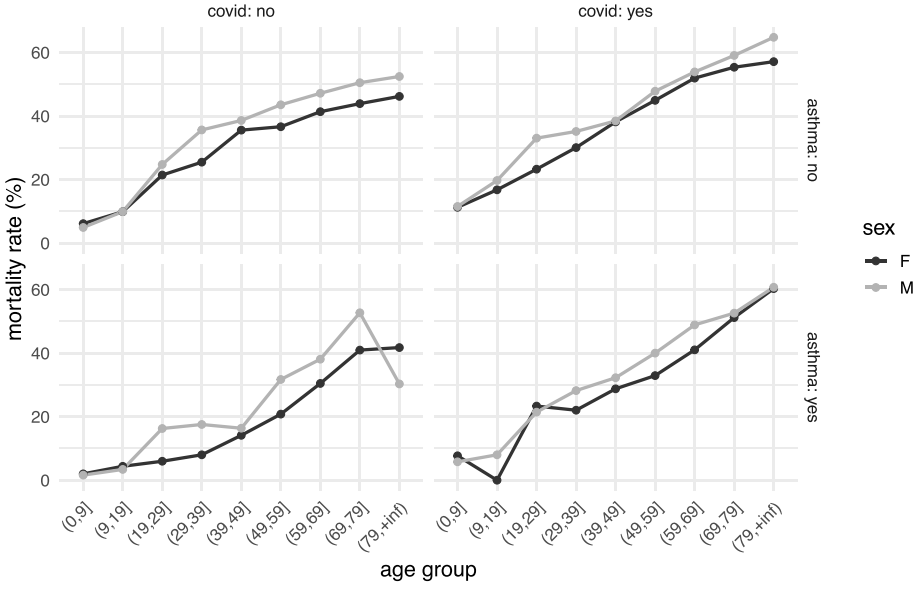

Fig. 4 Line plot of mortality rates of ICU patients by age group, asthma and COVID-19 status, and sex —female (F)/male (M)— with Brazilian data

predictors such as asthma control or comorbidity burden. Figure 6 explores this further by illustrating the age-specific prevalence of low O_2 saturation, stratified by asthma status and sex. Each curve employs a distinct line type for asthma status and varying shades of gray for sex, facilitating visual comparison.

Among males, the lowest prevalence of low O_2 saturation consistently occurs in the 19–29 age group, regardless of asthma diagnosis. In contrast, female non-asthmatics also exhibit their lowest prevalence in this same younger group (19–29 years), while asthmatic females reach their minimum prevalence slightly later, in the 29–39-year range. These subtle age-related differences may reflect underlying biological variation, differences in access or timing of care, or distinct comorbidity profiles, although further data would be required to confirm such hypotheses.

Given that our analysis does not include direct indicators of asthma severity or disease control (such as exacerbation frequency, dyspnea severity, or detailed respiratory support), caution is warranted when interpreting the observed mortality patterns. Incorporating variables related to asthma management—such as medication adherence, corticosteroid usage, or ventilatory support—would likely improve the understanding of why some patient subgroups experience low mortality

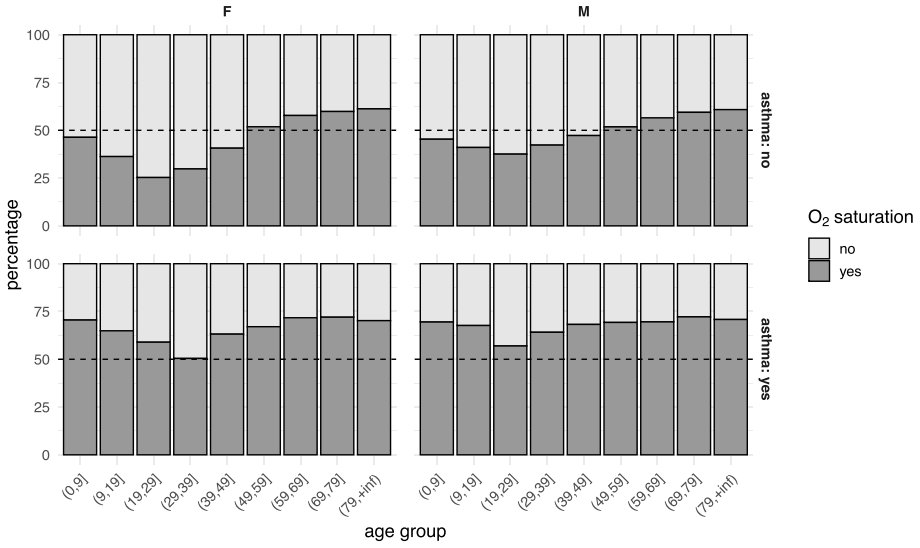

Fig. 5 Bar plot of percentage of patients with the indicated O_2 saturation level by age group and asthma status using Brazilian data

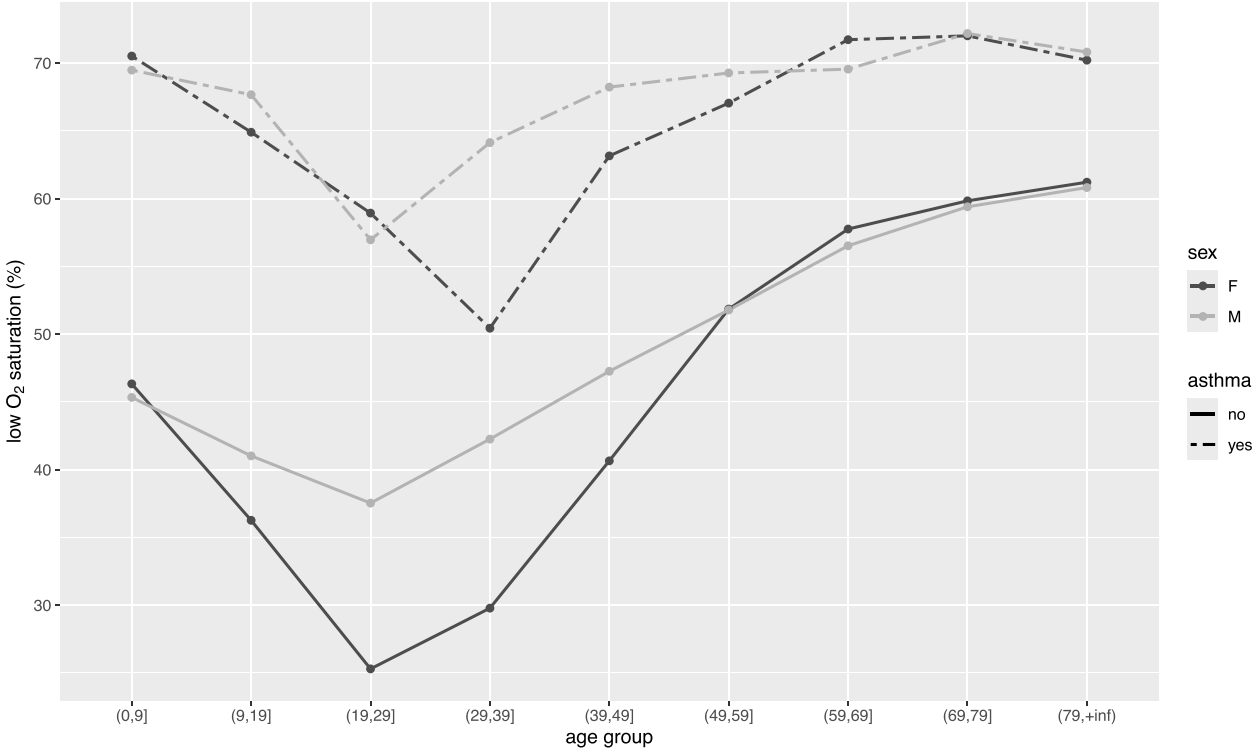

Fig. 6 Line plot of the proportion of patients with low O_2 saturation by age group, asthma status, and sex —female (F)/male (M)— using Brazilian data

despite presenting with signs of respiratory compromise. Future studies incorporating these variables may help to clarify the complex role of asthma in modulating SARI outcomes.

Logistic regression analyses

Based on the exploratory analysis, we constructed a logistic regression model incorporating main effects and selected higher-order interactions to explore patterns of SARI mortality. The model was refined using backward elimination, sequentially removing non-significant predictors and interactions while retaining those supported by clinical relevance. This approach yielded a more streamlined and interpretable model, preserving key predictors and interactions identified in the data.

Table 4 and Fig. 7 present the results for the refined frequentist and Bayesian models, including CrI for the Bayesian approach. This comparison

Table 4 Results of frequentist and Bayesian logistic regressions for SARI mortality, showing OR as well as lower and upper limits of CrIs using Brazilian data

			CrI	
Predictor	**OR**	**OR (Bayes)**	**Lower**	**Upper**
AGE(9,19]	2.4120	2.3632	1.8404	3.0042
AGE(19,29]	3.3414	3.2871	2.6912	4.0552
AGE(29,39]	5.9488	5.8709	4.9530	7.0287
AGE(39,49]	12.1285	11.9413	10.1757	14.0132
AGE(49,59]	14.0524	13.8738	11.9413	16.1190
AGE(59,69]	17.7154	17.4615	15.3329	20.0855
AGE(69,79]	21.8635	21.5419	18.9158	24.7791
AGE(79,+infinite)	38.4307	37.7128	33.4483	43.3801
ANTIVIRAL(yes)	0.6837	0.6839	0.6250	0.7483
ASTHMA(yes)	0.3083	0.3135	0.2187	0.4360
ASTHMA(Yes):AGE(9,19]	1.2164	1.1618	0.6188	2.1598
ASTHMA(yes):AGE(19,29]	2.2342	2.1383	1.1735	3.8574
ASTHMA(yes):AGE(29,39]	1.3743	1.3364	0.7945	2.2705
ASTHMA(yes):AGE(39,49]	1.4383	1.4049	0.8869	2.2255
ASTHMA(yes):AGE(49,59]	1.3553	1.3231	0.8694	2.0544
ASTHMA(yes):AGE(59,69]	1.5833	1.5527	1.0618	2.2933
ASTHMA(yes):AGE(69,79]	1.7648	1.7333	1.1972	2.6117
ASTHMA(yes):AGE(79,+infinite)	2.3471	2.2933	1.5999	3.3872
ASTHMA(yes):ICU(yes)	1.2132	1.2214	1.0101	1.4623
CFCLASS SARI (influenza)	0.5519	0.5488	0.4966	0.6126
CFCLASS SARI (not specified)	0.6832	0.6839	0.6637	0.7047
CFCLASS SARI (other etiologic agent)	1.0886	1.0833	0.9324	1.2586
CFCLASS SARI (other respiratory virus)	0.4566	0.4538	0.4066	0.5066
COVVAC(yes)	0.8228	0.8270	0.7945	0.8521
DYSPNEA(yes)	1.1131	1.1163	1.0833	1.1503
FLUVAC(yes)	0.7332	0.7334	0.6977	0.7711
ICU(Yes)	2.5768	2.5345	2.1598	2.9743
ICU(Yes):AGE(9,19]	0.7357	0.7558	0.5326	1.0725
ICU(yes):AGE(19,29]	1.1421	1.1618	0.8521	1.5841
ICU(yes):AGE(29,39]	0.8976	0.9139	0.6977	1.1972
ICU(yes):AGE(39,49]	0.6285	0.6376	0.4966	0.8106
ICU(yes):AGE(49,59]	0.7254	0.7408	0.5945	0.9139
ICU(yes):AGE(59,69]	0.7340	0.7483	0.6126	0.9048
ICU(yes):AGE(69,79]	0.7365	0.7483	0.6188	0.8958
ICU(yes):AGE(79,+infinite)	0.5553	0.5655	0.4724	0.6771
OXYGEN(yes invasive)	14.7255	14.7317	13.8738	15.6426
OXYGEN(yes non-invasive)	1.9635	1.9542	1.8965	2.0340
RESPDIS(yes)	1.2214	1.2214	1.1853	1.2586
SATUR(yes)	1.1248	1.1275	1.0833	1.1618
SEX(male)	0.8681	0.8607	0.7334	1.0101
SEX(male):AGE(9,19]	1.3435	1.3634	0.9900	1.8965
SEX(male):AGE(19,29]	2.7501	2.7732	2.1170	3.6693
SEX(male):AGE(29,39]	2.0040	2.0340	1.6000	2.5600
SEX(male):AGE(39,49]	1.2004	1.2092	0.9802	1.5068
SEX(male):AGE(49,59]	1.3932	1.4049	1.1503	1.7160
SEX(male):AGE(59,69]	1.4372	1.4477	1.1972	1.7333
SEX(male):AGE(69,79]	1.4902	1.5068	1.2586	1.8040
SEX(male):AGE(79,+infinite)	1.2901	1.3100	1.0942	1.5527
SEX(male):ICU(yes)	0.9922	1.0000	0.8025	1.2586
SEX(male):ICU(yes):AGE(19,29]	0.5257	0.5273	0.3465	0.8187

illustrates the consistency of key associations across both methodologies.

Overall, the comparison shows that age, ICU admission, and asthma status were among the most influential predictors across both frequentist and Bayesian approaches, underscoring the robustness of the main associations; see Table 4 and Fig. 7.

Remark (Bayesian CrI versus frequentist confidence intervals) In a frequentist framework, a 95% confidence interval is interpreted as follows: if the sampling process were repeated many times, 95% of the constructed intervals would contain the true parameter. In contrast, in the Bayesian framework, a 95% CrI reflects a 95% probability that the parameter lies within that interval, given the observed data and prior information. This probabilistic interpretation is often considered more intuitive by clinicians, as it directly expresses the uncertainty surrounding the parameter estimates.

Age-specific variations in the asthma–mortality association

Asthma was generally associated with lower odds of SARI mortality (main-effect OR = 0.308 in the frequentist model; OR = 0.3135, 95% CrI 0.2187–0.4360, in the Bayesian model). However, interaction terms (Table 4) show that this protective association is not uniform across age groups: it is markedly weaker in young adults (19–29 years) and in the very old (79 years and above).

For individuals aged 19–29, the interaction term ASTHMA(yes):AGE(19,29] was 2.23 (95% CrI: [1.17; 3.86]). Multiplying this by the main asthma effect yields a combined OR of approximately 0.69 compared with non-asthmatics of the same age—still below one, but much closer to one than in intermediate ages (OR $\approx$ 0.42–0.44 for 29–59 years). Thus, the lower odds of death for asthmatics is attenuated, not reversed, in early adulthood.

Among the oldest individuals (79 years and above), the interaction ASTHMA(yes):AGE(79,+infinite) was 2.35, resulting in a combined OR of about 0.72 versus non-asthmatics of the same age. The apparent protective association remains but is minimal, suggesting that advanced age and comorbidity burden nearly offset the expected benefit.

Several hypotheses might explain why protection wanes at the age extremes as follows:

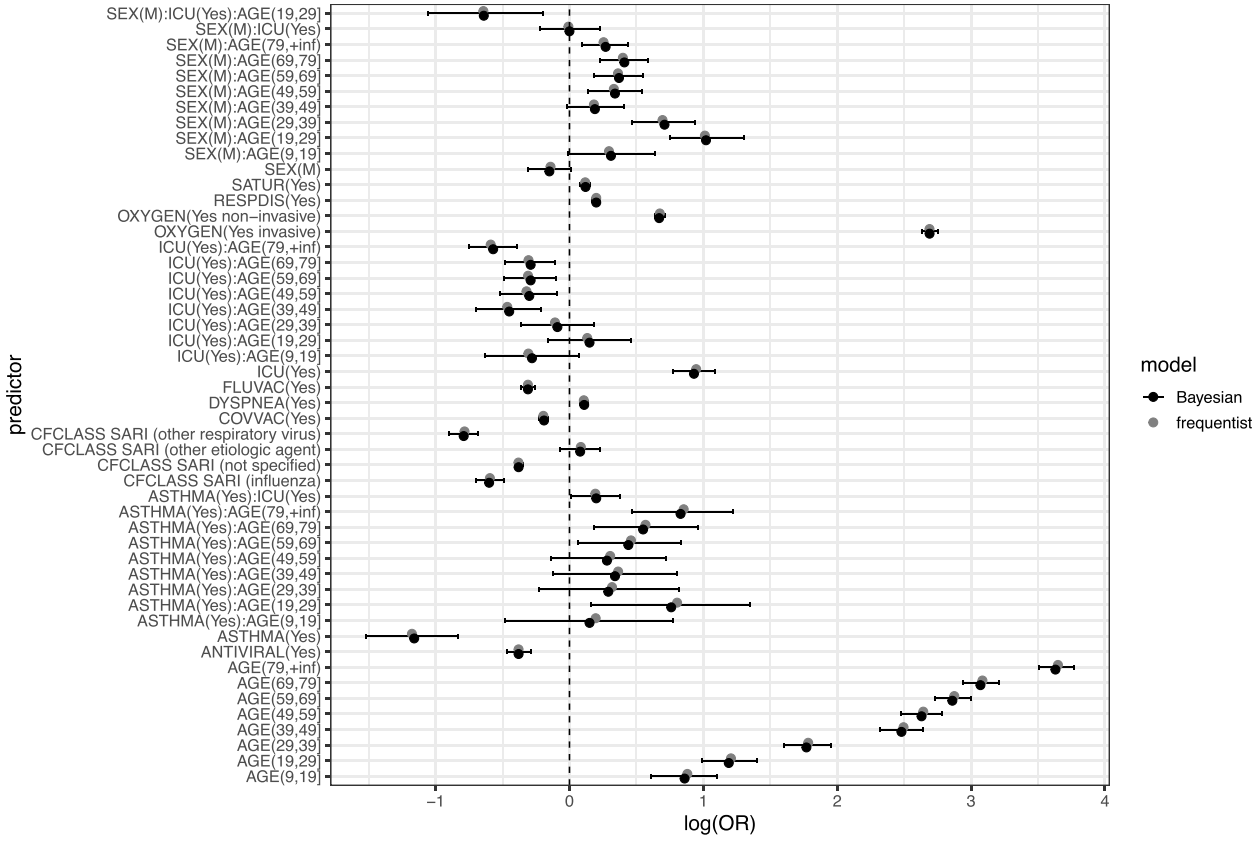

Fig. 7 Interval plots of $\log(\mathrm{OR})$ from frequentist (95% confidence intervals) and Bayesian (95% CrLs) logistic regressions for each predictor, based on Brazilian SARI data (2022)

- Medication adherence —Suboptimal use of controller therapy may be more common in young adults, but medication data were unavailable.
- Healthcare-seeking behavior —Delayed presentation could contribute, yet timing information was lacking.
- Biological variation —Age-specific phenotypes or immune responses may modify outcomes.
- Sociodemographic predictors —Greater mobility or occupational exposure in young adults, and frailty in the very old, could influence risk.

These findings emphasize the need for age-stratified management: enhanced surveillance of young adult asthmatics, who lose much of the usual survival advantage, and tailored care for the very elderly, in whom comorbidities and physiological decline further erode protection.

In addition to asthma-related effects, age alone was the dominant predictor of death. Among non-asthmatics, the adjusted OR of SARI mortality increased sharply, rising from about 3.34 in the 19–29 year group to 38.4 in those aged 79 years and above.

A noteworthy three-way interaction, SEX(male):ICU (yes):AGE(19,29], had an OR of 0.53. This suggests that the young male patients admitted to the ICU experienced lower mortality than would be expected based on the individual effects of sex, ICU admission, and age—possibly reflecting particularly effective intensive care or unmeasured protective predictors in this subgroup.

Additional salient coefficients included:

- ICU admission —Main-effect OR ≈ 2.58, confirming a substantial increase in mortality risk, partially modified by age and sex interactions.
- COVID-19 vaccination (COVVAC(yes)) — OR ≈ 0.82, corresponding to an 18% reduction in the adjusted OR of death.
- Oxygen support —The strongest single predictor of severity; invasive ventilation showed OR ≈ 14.7, while non-invasive support had OR ≈ 2.0.

Clinical and public health implications

These findings illustrate the heterogeneity of mortality risk in severe acute respiratory infection among people with asthma. Although an overall association with lower odds of death was observed, the magnitude of that association varied markedly: for adults aged 19–29 years and for those aged 79 years and above, the adjusted odds of death were only marginally lower than in non-asthmatics of the same age. Possible explanations—such as

differences in asthma control, access to timely care, phenotypic heterogeneity, or age-related immune variation—remain speculative because the present dataset lacks the necessary detail to test them.

Accordingly, risk-reduction strategies should not assume uniform protection in asthma. Rather, the present results suggest that:

- Surveillance and future research could focus on young adults with asthma (19–29 years) and on very old adults ($\geq$ 79 years), the two strata in which the survival advantage was least apparent.
- Age-stratified evaluation of vaccination programs and antiviral timing may help to clarify how these interventions modify mortality associations in high-risk subgroups.
- Critical-care pathways might benefit from further investigation of age–sex–asthma interactions before prescriptive changes in ICU triage are considered.

Because these conclusions derive from observational associations, they should be validated in prospective cohorts—including data on asthma severity, medication use, and socioeconomic context—before informing clinical guidelines.

Model performance and predictive accuracy

To assess the predictive effectiveness of our models, Table 5 presents various performance metrics for the logistic regression models. The results indicate that the models perform adequately in predicting mortality risk. Figure 8 illustrates this through the ROC-AUC, demonstrating good discrimination capability, with a ROC-AUC of 0.8448 and balanced between sensitivity and specificity in predicting SARI mortality. These indicators support the consistency of our analytical approach in identifying patterns among high-risk subgroups.

Table 5 Values of model performance metrics and their interpretation for logistic regression models with Brazilian data

Metric	Value	Interpretation
Accuracy	0.7512	Overall prediction accuracy
Sensitivity (recall)	0.7373	Ability to correctly identify mortality cases
Specificity	0.7670	Ability to correctly identify non-mortality cases
Precision	0.7837	Reliability of high-risk predictions
F1 score	0.7598	Balance of precision and recall
ROC-AUC	0.8448	Overall model discrimination capability
Negative predictive value	0.7512	Reliability of non-mortality predictions
False positive rate	0.2330	Rate of false-positive mortality predictions
Balanced accuracy	0.7521	Average of sensitivity and specificity

While the primary goal of our logistic regression models was to interpret associations between variables and SARI mortality, the performance metrics offer additional support for the model's ability to identify high-risk patients. The observed discriminatory capacity and balance between sensitivity and specificity suggest that the model captures relevant structure in the data without overfitting.

Discussion

In this section, clinical implications, study limitations, and directions for future research are discussed.

Age-specific impacts of asthma

The main effect of ASTHMA(yes) (OR $\approx$ 0.31) indicated substantially reduced mortality OR overall. However, interaction terms in Table 4 show that this favorable association is not uniform across age brackets, as follows:

- Young adults (19–29 years) —In this group, the interaction term ASTHMA(yes):AGE(19,29] (OR $\approx$ 2.23) markedly diminishes the survival advantage of asthma. When compared with non-asthmatics of the same age, asthmatics still had low OR of death (combined OR $\approx$ 0.69), but the protection is far smaller than that seen in intermediate ages. Conversely, when referenced to asthmatic children (0–9 years), mortality is around 7.5-fold higher, indicating that young adults with asthma represent a relative "gap" in the usual age-risk gradient and warrant focused study of adherence, disease control, and access to care.
- Elderly adults (over 79 years) —The interaction ASTHMA(yes):AGE(79,+infinite) (OR $\approx$ 2.35) similarly attenuates the protective association, yielding a combined OR $\approx$ 0.72 versus non-asthmatics of the same age. Although asthma is still linked to slightly low OR of death, the difference is minimal, suggesting that advanced age, comorbidity burden, and physiological decline largely outweigh any benefit usually observed in asthmatic patients.

Vaccination and unadjusted versus adjusted mortality

Early descriptive results showed high unadjusted mortality among vaccinated individuals (28% versus 12.9% in non-asthmatics, 14.5% versus 4.5% in asthmatics). At first glance, this might appear to contradict the expected protective association of vaccination. However, vaccination prioritization was given to older individuals and those with comorbid conditions [34, 35], introducing a strong confounding effect. Table 3 shows that vaccinated groups include a disproportionate number of high-risk individuals.

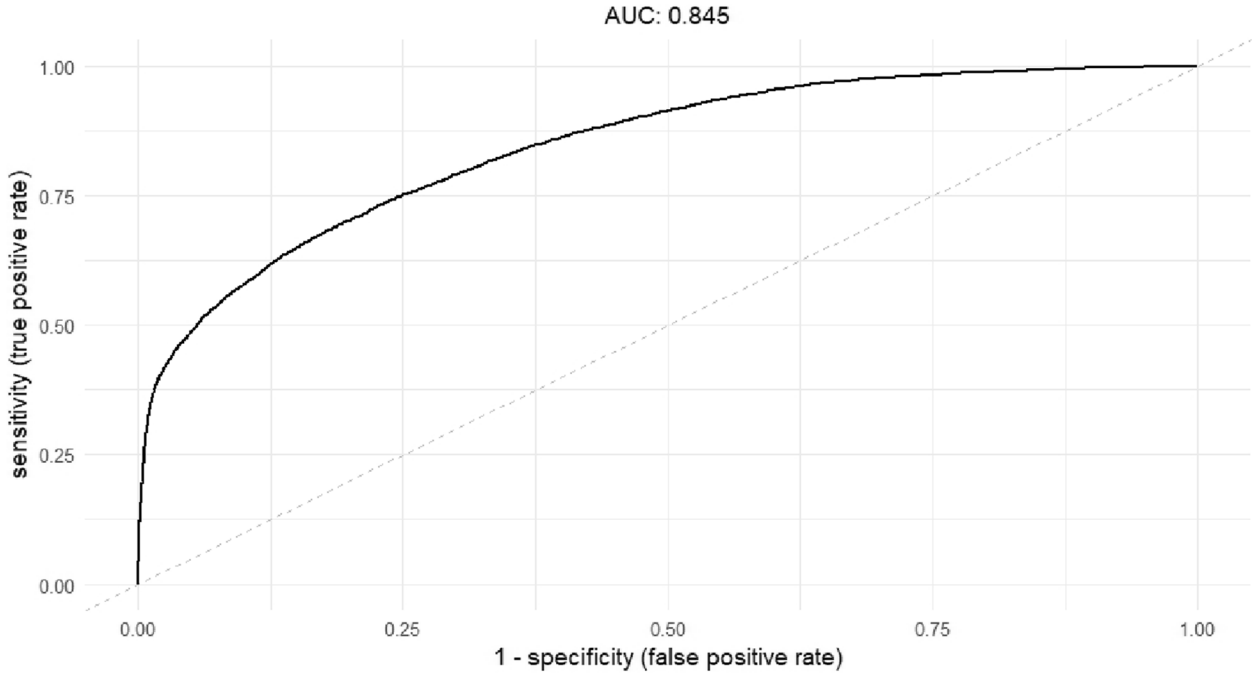

Fig. 8 ROC-AUC for the logistic regression model with Brazilian asthma data

Figure 2 illustrates that, from age 19–29 onwards, unvaccinated individuals have greater mortality rates than vaccinated ones, both in asthmatic and non-asthmatic subpopulations. This pattern aligns with the notion that crude mortality comparisons can be misleading when the distribution of key predictors (such as age or comorbidities) differs between vaccinated and unvaccinated groups.

In our multivariable logistic regression, after adjusting for ICU admission, age, and selected comorbidities, COVVAC(Yes) was associated with approximately an 18% lower limit for OR of mortality (OR ≈ 0.82). A similar association was observed for influenza vaccination. These results highlight that observational analyses of vaccine effectiveness require careful adjustment for confounding and support the potential value of immunization in high-risk populations.

Therefore, while the raw data may initially suggest high mortality among vaccinated individuals, closer examination indicates that vaccination is associated with low mortality risk after appropriate adjustments. This emphasizes the need for caution when interpreting unadjusted comparisons in observational studies evaluating vaccine impact.

Role of intensive care unit admission

ICU admission was associated with substantially increased odds of mortality (adjusted OR ≈ 2.58). Nevertheless, interaction terms revealed a more nuanced pattern, as follows:

- Middle-aged patients (39–59) —These individuals appeared to experience better outcomes with ICU care than younger or older patients, possibly due to low comorbidity burden or high physiological reserve, although these predictors were not directly measured.
- Young males in ICU — The three-way interaction indicated that young male ICU patients (19–29 years) had slightly lower odds of mortality than would be expected from the pairwise effects (adjusted OR lower than predicted), which may reflect differences in clinical response or unmeasured factors specific to this subgroup.

Overall, ICU admission remained a strong indicator of severe illness, yet certain demographic subgroups may exhibit differential outcomes following intensive care.

Antiviral use and oxygen saturation

Although antiviral treatment was associated with lower mortality, the observational nature of the dataset limits the ability to draw causal inferences.

By contrast, low oxygen saturation (SATUR = *yes*) consistently emerged as a strong predictor of increased odds of mortality, with important interactions by asthma status, age, and sex. Notably, although asthmatic patients frequently presented with low O_2 saturation, they did not uniformly experience higher mortality.

This observation suggests that the relationship between oxygen saturation and mortality in asthmatic patients

Table 6 Adjusted OR (95% CI) for ASTHMA(yes) within each oxygen-support stratum

O_2 stratum	N (deaths)	OR for asthma	95% CI
No support	112,756 (9,282)	0.47	(0.39, 0.56)
Non-invasive	254,025 (48,420)	0.54	(0.51, 0.58)
Invasive	48,930 (32,368)	0.59	(0.53, 0.66)

may be modulated by other unmeasured predictors, such as disease control, treatment adherence, or physiological characteristics. However, the present data do not include direct information on these variables, and the observed associations should be interpreted accordingly.

To explore whether the association between asthma and mortality varied according to clinical severity —particularly the level of respiratory support required— we performed an additional subgroup analysis stratified by oxygen therapy intensity, as outlined below.

Post-hoc analysis stratified by oxygen therapy

Our primary analysis adjusted for respiratory support (OXYGEN: no, yes_non_invasive, yes_invasive) as a predictor. However, recognizing that oxygen therapy intensity may indirectly reflect clinical severity, we performed an additional targeted post-hoc analysis, stratifying patients explicitly by their required level of respiratory support. This allowed us to assess whether the association between asthma and mortality remained consistent across different levels of respiratory distress.

We divided the dataset into three strata according to oxygen therapy level as follows:

- No oxygen support —112,756 patients with an overall mortality of 8.2% (9,282 deaths).
- Non-invasive support —254,025 patients with an overall mortality of 19.1% (48,420 deaths).
- Invasive support —48,930 patients with an overall mortality of 66.2% (32,368 deaths).

Within each stratum, logistic regression models were refitted using the same set of predictors described in "Logistic regression analyses" section, excluding the variable OXYGEN, as all individuals within each subgroup shared identical oxygen-support status. Table 6 summarizes the adjusted OR and corresponding 95% confidence intervals for mortality associated with ASTHMA(yes) in each oxygen-support subgroup.

In all three strata, asthma was consistently associated with lower odds of mortality, with adjusted ORs ranging from approximately 0.47 (no oxygen support) to 0.59 (invasive support). Notably, even among patients requiring invasive ventilation—who exhibited the highest baseline mortality rate (66.2%)—asthmatic patients showed a lower adjusted OR for death than non-asthmatic patients. These patterns align with the findings of our main analysis ("Logistic regression analyses" section), in which asthma was generally associated with reduced mortality risk.

Nevertheless, interpretation of these results requires caution due to the potential for residual confounding. In particular, patients receiving invasive ventilation likely present with complex clinical profiles and comorbidities that may influence outcomes independently of asthma. Additionally, the categorical classification of oxygen support does not capture the full spectrum of asthma severity or control. Future research incorporating clinical variables such as inhaled corticosteroid use, frequency of asthma exacerbations, or objective lung function measures would be valuable in clarifying the relationship between asthma control, phenotype, and mortality across different levels of respiratory compromise.

Practical implications

Our results indicate that age, comorbidities, and ICU admission jointly shape the association between asthma and in-hospital mortality, cautioning against the assumption that asthma is uniformly protective. They suggest the following priorities for further investigation and potential service planning:

- Young adults with asthma (19–29 years) —Often regarded as low-risk, this group shows a markedly smaller survival advantage than children and middle-aged adults and therefore merits closer epidemiological follow-up.
- Very old adults with asthma ($\geq$ 79 years) —Frailty and multimorbidity almost eliminate the advantage observed at younger ages, underscoring the need to understand how geriatric factors modify SARI outcomes in this population.
- Vaccination and early antiviral therapy —The adjusted analyses support an association with lower mortality, but crude comparisons can be misleading when age and comorbidities are not taken into account.
- ICU triage and management —Some demographic subgroups (such as young adult males) may respond differently to intensive interventions, suggesting value in examining age-, sex-, and phenotype-specific critical-care pathways.

These associations require confirmation in prospective, well-phenotyped cohorts before they can inform clinical guidelines. Further work should incorporate adherence, asthma phenotype, and other unmeasured modifiers of severe respiratory outcomes.

Limitations

While this study provides valuable insights, it is subject to several limitations as follows:

- Assumptions of logistic regression models —Neither frequentist nor Bayesian logistic regression requires the absence of multicollinearity; strong collinearity mainly inflates standard errors and can hamper interpretability but does not, by itself, bias coefficient estimates. Key assumptions remain (i) correct specification of the logit link, (ii) independence of observations, and (iii) approximate linearity of the log-odds for any continuous covariates. Even when categorical predictors are highly correlated, the principal consequence is loss of precision rather than model invalidation [38]. Given our large sample, we expect any loss of precision to have had only a minor impact on the main findings.
- Potential misclassification of SARI subtypes —A high proportion of our dataset falls under the "not specified" SARI category, which could mask cases of influenza, COVID-19, or other respiratory viruses. This incomplete or inaccurate classification may introduce bias if certain subtypes were systematically under- or over-reported.
- Unmeasured confounders —Despite adjustment for multiple predictors, several important variables remained unmeasured. For example, key variables such as obesity and smoking status (both established risk factors for severe respiratory outcomes) were not consistently captured in the dataset. Additionally, variables such as healthcare access, detailed socioeconomic status, regional disparities, and treatment adherence may also influence the relationship between asthma and SARI mortality, potentially introducing residual confounding.
- Regional differences —Although our dataset includes a variable identifying the five Brazilian regions, we did not perform a region-stratified analysis in this study. This decision was based on the substantial heterogeneity between regions in terms of socioeconomic status, healthcare access, population density, and resource availability, which would require extensive, region-specific adjustments to reliably interpret results. Future studies that explicitly address regional heterogeneity may further improve our understanding of socioeconomic and geographic disparities.
- Generalizability limitations —Our findings derive from nationwide data encompassing both public and private healthcare systems in Brazil, providing insights specific to the Brazilian context. Therefore, results may not be directly generalizable to countries with different healthcare infrastructures, demographic characteristics, or epidemiological profiles.
- Evolution of COVID-19 factors over time —The study does not explicitly account for temporal variations in COVID-19-related treatment protocols, viral mutations, or vaccination campaigns, which could affect mortality risk. Additionally, detailed timing information for interventions such as vaccinations and antiviral treatments was not consistently available, potentially influencing the associations observed.
- Data balancing considerations —We conducted sensitivity analyses using several data balancing methods (SMOTE, oversampling, and undersampling). Undersampling was ultimately selected to minimize artificial outcome distribution alteration. However, this method reduces the majority class sample size. While this choice was methodologically justified to preserve internal validity, it may modestly affect generalizability.
- Observational nature of the study —Findings reflect associations, not causality, as is characteristic of retrospective observational designs. Prospective and controlled studies would be necessary to confirm and clarify these associations.

Future directions

The previously mentioned limitations could be addressed by the following:

- Exploring detailed interactions –Further investigation into the interactions among asthma, comorbidities, and therapeutic interventions could help to develop refined risk profiles. For instance, evaluating asthma severity in conjunction with treatment adherence and COVID-19-related outcomes may provide more nuanced insights.
- Integrating additional variables –Incorporating environmental factors, healthcare access, socioeconomic status, and treatment adherence into the modeling framework could help to control for potential confounders and improve model precision.
- Validating models across different healthcare settings –Generalization and robustness assessments could be enhanced by validating the developed models using data from diverse healthcare environments. Cross-validation techniques and independent cohort studies may further strengthen model applicability.
- Conducting longitudinal studies –Prospective research could offer insights into the long-term effects of asthma on SARI outcomes, providing a more comprehensive understanding of how chronic conditions influence recovery trajectories.

- Investigating biological mechanisms – Complementary studies examining airway inflammation, asthma medication effects, and immune response variability could help to elucidate the pathways through which asthma influences SARI severity.
- Exploring advanced machine learning techniques –While our study focused on interpretable models, future research may consider approaches such as gradient boosting, neural networks, and random forests to detect complex patterns. However, balancing these methods with model interpretability remains essential. Techniques such as Shapley additive explanations or local interpretable model-agnostic explanations could enhance transparency and reveal patterns not captured by simpler models, potentially improving clinical applicability [42, 43]. Recent applications of these methods in clinical datasets further highlight their potential to improve the interpretability and usability of complex models in healthcare settings [41].

Summary of the discussion

The multivariable models identified age and ICU admission as the strongest predictors of SARI mortality, in line with previous studies [27]. Asthma was generally associated with lower odds of death, but this association was strongly modified by age, emphasizing the need for age-stratified research rather than one-size-fits-all management strategies.

Conclusions

We analyzed 415,711 hospital admissions for severe acute respiratory infection recorded in Brazil in 2022. After addressing class imbalance by random undersampling, we fitted frequentist and Bayesian logistic regression models to assess the relationship between asthma, age, and other clinical predictors and in-hospital mortality. The final model displayed good discrimination (ROC-AUC 0.845; sensitivity 0.74; specificity 0.77).

Age was the dominant predictor: compared with children aged 0–9 years, the adjusted odds of death rose to approximately 38 among patients aged 79 years or older. Asthma showed an overall protective association (adjusted OR $\approx$ 0.31), but this association weakened in young adults (19–29 years, OR $\approx$ 0.69) and in the very old ($\geq$79 years, OR $\approx$ 0.72). Vaccination against COVID-19 or influenza was associated with lower mortality (OR $\approx$ 0.82), whereas ICU admission increased it (main-effect OR $\approx$ 2.6). Invasive mechanical ventilation remained the single strongest clinical marker of severity (OR $\approx$ 14.7). The protective association of asthma persisted among mechanically ventilated patients (adjusted OR $\approx$ 0.59).

These age-specific associations highlight hypotheses for future research—particularly regarding asthmatics aged 19–29 and $\geq$79 years—and suggest the potential value of vaccination and early antiviral therapy in all high-risk groups. The Bayesian analysis complements traditional estimates by quantifying parameter uncertainty.

Key limitations include the absence of data on asthma control, medication adherence, smoking status, obesity, and socioeconomic conditions, which may result in residual confounding. Prospective studies with richer clinical detail and external validation in other healthcare systems are essential before these associations can inform changes in clinical practice or policy.

Acknowledgements
The authors thank anonymous reviewers for their comments and suggestions, which have contributed to improving the clarity and quality of the article.

Authors' contributions
Cecilia Castro (CC), Víctor Leiva (VL), and Viviana Giampaoli (VG) conceived the study and developed the research concept. VG provided the dataset and was responsible for data acquisition and preprocessing. CC, VL, VG, Diana Prieto (DP), and Carlos Martin-Barreiro (CMB) performed the data analyses and contributed equally to the interpretation of the results. Johanna Viana (JV) provided clinical insights and contributed to the interpretation of medical implications. CC and VL drafted the article. All authors critically revised the article for intellectual content and approved the final version for submission.

Funding
CC gratefully acknowledges partial financial support from the Centro de Matemática da Universidade do Minho, Portugal, through UID/00013.

Data availability
The dataset supporting this study is publicly available through the Brazilian Ministry of Health's open data repository at: https://opendatasus.saude.gov.br/dataset/srag-2021-a-2024. Note that SIVEP-Gripe data are regularly updated so that exact numbers might vary in subsequent downloads.

Declarations

Ethics approval and consent to participate
This study used publicly available, anonymized secondary data from the Brazilian Ministry of Health SIVEP-Gripe system. According to Brazilian regulations (Resolution CNS 510/2016) and the General Data Protection Law (Lei nº 13.709/2018), the use of anonymized public data does not require ethical approval or informed consent.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Author details
[1]Centre of Mathematics, Universidade do Minho, Braga, Portugal
[2]School of Industrial Engineering, Pontificia Universidad Católica de Valparaíso, Valparaíso, Chile
[3]Institute of Mathematics and Statistics, Universidade de São Paulo, São Paulo, Brazil
[4]Facultad de Ciencias Naturales y Matemáticas, Escuela Superior Politécnica del Litoral, Guayaquil, Ecuador
[5]Department of Nephrology, Unidade de Saúde Local de Braga, Braga, Portugal

Received: 31 January 2025 / Accepted: 1 August 2025
Published online: 30 September 2025

References

1. Murray CJL. Findings from the global burden of disease study 2021. Lancet. 2024;403:2259–62. https://doi.org/10.1016/S0140-6736(24)00769-4.
2. Walters GI, Reilly C, Le Moual N, Huntley CC, Hussein H, Marsh J, et al. Asthma control in severe asthma and occupational exposures to inhalable asthmagens. BMJ Open Respir Res. 2024;11: e001943. https://doi.org/10.1136/bmjresp-2023-001943.
3. Levy ML, Bacharier LB, Bateman E, Boulet LP, Brightling C, Buhl R, et al. Key recommendations for primary care from the 2022 Global Initiative for Asthma (GINA) update. NPJ Prim Care Respir Med. 2023;33:1–13. https://doi.org/10.1038/s41533-023-00330-1.
4. Global Initiative for Asthma (GINA). Global strategy for asthma management and prevention. 2024. https://ginasthma.org/2024-gina-report/. Accessed 30 June 2025.
5. Urrutia-Pereira M, Mocelin LP, Ellwood P, Garcia-Marcos L, Simon L, Rinelli P, et al. Prevalence of rhinitis and associated factors in adolescents and adults: a Global Asthma Network study. Rev Paul Pediatr. 2023;41: e2021400. https://doi.org/10.1590/1984-0462/2023/41/2021400.
6. Votto M, De Silvestri A, Postiglione L, De Filippo M, Manti S, La Grutta S, et al. Predicting paediatric asthma exacerbations with machine learning: a systematic review with meta-analysis. Eur Respir Rev. 2024;33(174): 240118. https://doi.org/10.1183/16000617.0118-2024.
7. Tomita K, Nagao R, Touge H, Ikeuchi T, Sano H, Yamasaki A, et al. Deep learning facilitates the diagnosis of adult asthma. Allergol Int. 2019;68:456–61. https://doi.org/10.1016/j.alit.2019.04.010.
8. Luo G, Nkoy FL, Stone BL, Schmick D, Johnson MD. A systematic review of predictive models for asthma development in children. BMC Med Inform Decis Mak. 2015;15:99. https://doi.org/10.1186/s12911-015-0224-9.
9. Ospina R, Ferreira AGO, Oliveira HM, Leiva V, Castro C. On the use of machine learning techniques and non-invasive indicators for classifying and predicting cardiac disorders. Biomedicines. 2023;11: 2604. https://doi.org/10.3390/biomedicines11102604.
10. Taylan O, Alkabaa AS, Alqabbaa HS, Pamukcu E, Leiva V. Early prediction in classification of cardiovascular diseases with machine learning, neuro-fuzzy and statistical methods. Biology. 2023;12: 117. https://doi.org/10.3390/biology12010117.
11. Sardar I, Akbar MA, Leiva V, Alsanad A, Mishra P. Machine learning and automatic ARIMA/Prophet models-based forecasting of COVID-19: methodology, evaluation, and case study in SAARC countries. Stoch Environ Res Risk Assess. 2023;37:345–59. https://doi.org/10.1007/s00477-022-02307-x.
12. Castro C, Leiva V, Garrido D, Huerta M, Minatogawa V. Blockchain in clinical trials: Bibliometric and network studies of applications, challenges, and future prospects based on data analytics. Comput Methods Programs Biomed. 2024;255:108321. https://doi.org/10.1016/j.cmpb.2024.108321.
13. Seol HY, Shrestha P, Muth JF, Wi CI, Sohn S, Ryu E, et al. Artificial intelligence-assisted clinical decision support for childhood asthma management: a randomized clinical trial. PLoS One. 2021;16:e0255261. https://doi.org/10.1371/journal.pone.0255261.
14. Kaplan A, Cao H, FitzGerald JM, Iannotti N, Yang E, Kocks JWH, et al. Artificial intelligence/machine learning in respiratory medicine and potential role in asthma and COPD diagnosis. J Allergy Clin Immunol Pract. 2021;9:2255–61. https://doi.org/10.1016/j.jaip.2021.02.014.
15. Spyroglou II, Spock G, Chatzimichail EA, Rigas AG, Paraskakis EN. A Bayesian logistic regression approach in asthma persistence prediction. Epidemiol Biostat Public Health. 2018;15:1–9. https://doi.org/10.2427/12777.
16. Cobian A, Abbott M, Sood A, Sverchkov Y, Hanrahan L, Guilbert T, et al. Modeling asthma exacerbations from electronic health records. AMIA Summits Transl Sci Proc. 2020;2020:98–107. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7233095/. Accessed 30 June 2025.
17. Martin A, Bauer V, Datta A, Masi C, Mosnaim G, Solomonides A, Rao G. Development and validation of an asthma exacerbation prediction model using electronic health record data. J Asthma. 2020;57:1339–46. https://doi.org/10.1080/02770903.2019.1648505.
18. Boer S, Sont JK, Loijmans RJB, Snoeck-Stroband JB, Ter Riet G, Schermer TRJ, et al. Development and validation of personalized prediction to estimate future risk of severe exacerbations and uncontrolled asthma. J Allergy Clin Immunol Pract. 2019;7:175–82. https://doi.org/10.1016/j.jaip.2018.06.007.
19. Daines L, McLean S, Buelo A, Lewis S, Sheikh A, Pinnock H. Systematic review of clinical prediction models to support the diagnosis of asthma in primary care. NPJ Prim Care Respir Med. 2019;29: 19. https://doi.org/10.1038/s41533-019-0132-z.
20. Feng Y, Wang Y, Zeng C, Mao H. Artificial intelligence and machine learning in chronic airway diseases: focus on asthma and chronic obstructive pulmonary disease. Int J Med Sci. 2021;18:2871–80. https://doi.org/10.7150/ijms.58191.
21. Molfino NA, Turcatel G, Riskin D. Machine learning approaches to predict asthma exacerbations: a narrative review. Adv Ther. 2024;41:534–52. https://doi.org/10.1007/s12325-023-02743-3.
22. Mekov E, Miravitlles M, Petkov R. Artificial intelligence and machine learning in respiratory medicine. Expert Rev Respir Med. 2020;14:559–64. https://doi.org/10.1080/17476348.2020.1743181.
23. Bustos N, Tello M, Droppelmann G, Garcia N, Feijoo F, Leiva V. Machine learning techniques as an efficient alternative diagnostic tool for COVID-19 cases. Signa Vitae. 2022;18:23–33. https://doi.org/10.22514/sv.2021.110.
24. Alkady W, ElBahnasy K, Leiva V, Gad W. Classifying COVID-19 based on amino acids encoding with machine learning algorithms. Chemometr Intell Lab Syst. 2022;224: 104535. https://doi.org/10.1016/j.chemolab.2022.104535.
25. Rahman MZU, Akbar MA, Leiva V, Martin-Barreiro C, Imran M, Riaz MT, et al. An IoT-fuzzy intelligent approach for holistic management of COVID-19 patients. Heliyon. 2024;10:e22454. https://doi.org/10.1016/j.heliyon.2023.e22454.
26. Bosnic-Anticevich S, Bakerly ND, Chrystyn H, Hew M, van der Palen J. Advancing digital solutions to overcome longstanding barriers in asthma and COPD management. Patient Prefer Adherence. 2023;17:259–72. https://doi.org/10.2147/PPA.S385857.
27. Milucky J, Pondo T, Gregory CJ, Iuliano D, Chaves SS, McCracken J, et al. The epidemiology and estimated etiology of pathogens detected from the upper respiratory tract of adults with severe acute respiratory infections in multiple countries, 2014–2015. PLoS One. 2020;15: e0240309. https://doi.org/10.1371/journal.pone.0240309.
28. Boussarsar M, Ennouri E, Habbachi N, Bouguezzi N, Meddeb K, Gallas S, et al. Epidemiology and burden of severe acute respiratory infections (SARI) in the aftermath of the COVID-19 pandemic: a prospective sentinel surveillance study in a Tunisian medical ICU, 2022/2023. PLoS ONE. 2023;18:e0294960. https://doi.org/10.1371/journal.pone.0294960.
29. Qin SX, Cheng FWT, Kwok WC, Fung LWY, Ma TT, Yiu HHE, et al. Effectiveness and respiratory adverse events following inactivated and mRNA COVID-19 vaccines in patients with COPD and asthma: a Chinese population-based study. Drug Saf. 2024;47:135–46. https://doi.org/10.1007/s40264-023-01364-7.
30. Mohamed AM, Al Sayyad A, Matar E, Isa HM, Hasan WF, Hashim NSJY, et al. Factors associated with poor outcomes in patients with severe acute respiratory infections in Bahrain. Influenza Other Respir Viruses. 2023;17: e13133. https://doi.org/10.1111/irv.13133.
31. Leal LF, Merckx J, Fell DB, Kuchenbecker R, Miranda AE, de Oliveira WK, et al. Characteristics and outcomes of pregnant women with SARS-CoV-2 infection and other severe acute respiratory infections (SARI) in Brazil from January to November 2020. Braz J Infect Dis. 2021;25: 101620. https://doi.org/10.1016/j.bjid.2021.101620.
32. Hassan MZ, Islam MA, Shoshi HR, Hossain MK, Shirin T, Chowdhury F. Characterizing deaths among adult patients with severe acute respiratory infection during the pre- and COVID-19 pandemic periods in Bangladesh, 2018–2022. Trop Med Health. 2023;51: 70. https://doi.org/10.1186/s41182-023-00565-1.
33. Peng B, Xiong Y, Ouyang T, He Q, Qi S, Yang Z, et al. High ratio of epi-25-(OH)-vitamin D3 to 25-(OH)-vitamin D3 increases the risk of asthma attack in American asthma adults: a population study. BMC Public Health. 2024;24:2670. https://doi.org/10.1186/s12889-024-20185-6.
34. Islam MA, Hassan MZ, Aleem MA, Akhtar Z, Chowdhury S, Ahmmed MK, et al. Post-discharge mortality among patients hospitalised with severe acute respiratory infection, Bangladesh, 2012–2019: a prospective observational study. Lancet Reg Health. 2024; 100363. https://doi.org/10.1016/j.lansea.2024.100363.
35. Elhassan UEA, Mohamed SAA, Rizk MS, Sherif M, El-Harras M. Outcomes of patients with severe acute respiratory infections (SARI) admitted to the intensive care unit: results from the Egyptian surveillance study 2010–2014. Multidiscip Respir Med. 2020;15: 465. https://doi.org/10.4081/mrm.2020.465.
36. Brazilian Ministry of Health. Severe acute respiratory infections data – 2021 and 2022. https://opendatasus.saude.gov.br/dataset/srag-2021-a-2024. Accessed 30 June 2025.
37. Galea M, Catalán M, Tapia A, Giampaoli V, Leiva V. Improving the modeling of binary response regression based on new proposals for statistical diagnostics with applications to medical data. Stat Med. 2025;44(13–14):e70073. https://doi.org/10.1002/sim.70073.
38. Gelman A, Carlin JB, Stern HS, Rubin DB. Bayesian data analysis. London: Chapman and Hall/CRC; 1995.

39. He H, Garcia EA. Learning from imbalanced data. IEEE Trans Knowl Data Eng. 2009;21:1263–84. https://doi.org/10.1109/TKDE.2008.239.
40. Chawla NV, Bowyer KW, Hall LO, Kegelmeyer WP. SMOTE: synthetic minority over-sampling technique. J Artif Intell Res. 2002;16:321–57. https://doi.org/10.1613/jair.953.
41. Rahnama AHA, Galera Alfaro L, Wang Z, Movin M. Local interpretable model-agnostic explanations for neural ranking models. Linköping Electronic Conference Proceedings. 2024. https://doi.org/10.3384/ecp208017.
42. Ribeiro MT, Singh S, Guestrin C. Why should I trust you? Explaining the predictions of any classifier. In: Proceedings of the 22nd International Conference on Knowledge Discovery and Data Mining. 2016. pp. 1135–44. https://doi.org/10.1145/2939672.2939778.
43. Nohara Y, Matsumoto K, Soejima H, Nakashima N. Explanation of machine learning models using Shapley additive explanation and application for real data in hospital. Comput Methods Programs Biomed. 2022;214: 106584. https://doi.org/10.1016/j.cmpb.2021.106584.
44. Martin-Barreiro C, Cabezas X, Leiva V, Ramos de Santis P, Ramirez-Figueroa JA, Delgado E. Statistical characterization of vaccinated cases and deaths due to COVID-19: methodology and case study in South America. AIMS Math. 2023;8:22693–713. https://doi.org/10.3934/math.20231155.
45. National Supplementary Health Agency (ANS). General data on Brazilian supplementary health sector (December 2024). https://www.gov.br/ans/pt-br/acesso-a-informacao/perfil-do-setor/dados-gerais. Accessed May 2025

Publisher's Note

Cecilia Castro — Assistant Professor of Statistics and Mathematics at Universidade do Minho, Portugal Cecilia Castro received the Ph.D. degree in sciences from Universidade do Minho, Braga, Portugal, in 2002. She is currently an Assistant Professor with Universidade do Minho and a member of the Centre of Mathematics. She has coauthored more than 50 peer-reviewed publications in these areas, contributing both to methodological development and to applications across diverse domains. Her research interests include statistical methodology, mathematical statistics, and data science, with a focus on current topics, such as dependence modeling, uncertainty quantification, interpretable machine learning, and high-dimensional inference. She is a member of the Portuguese Statistical Society and serves as a reviewer for several international journals. She frequently presents her work at international conferences, both through peer-reviewed contributions and invited presentations. She is one of the Editors-in-Chief of Chilean Journal of Statistics and serves on the editorial boards of several other scientific journals.

Víctor Leiva — Full Professor of Statistics and Data Science at Pontificia Universidad Católica de Valparaíso, Chile Víctor Leiva received the degree in statistics from Pontificia Universidad Católica de Valparaíso, Chile, and the Ph.D. degree in statistics and operational research from the University of Granada, Spain. He completed a postdoctoral fellowship in data science for business and industry at McMaster University, Canada. Currently, he is a Full Professor at the School of Industrial Engineering, Pontificia Universidad Católica de Valparaíso. He is an internationally recognized researcher and an Elected Member of the International Statistical Institute (ISI). His research has been continuously funded by the National Agency for Research and Development (ANID) of the Chilean Ministry of Science, Technology, Knowledge, and Innovation through FONDECYT project grants, receiving outstanding evaluations for 21 consecutive years. He has published approximately 300 scientific articles in leading international journals. His research interests include artificial intelligence, big data, data science, machine learning, multivariate statistical analysis, non-Gaussian statistical distributions, operational research, quality control, and statistical modeling. His contributions have earned him numerous honors and awards. In 2013, he served on the prestigious Karl Pearson Prize Selection Committee, considered the "Nobel Prize of Statistics," awarded by the ISI. In 2021, 2022, 2023, and 2025 (released in 2025) https://research.com ranked him as the #1 top scientist in mathematics and statistics in Chile. His H-index is 56 (Google Scholar), 49 (Scopus), and 48 (Web of Science). He is one of the Editors-in-Chief of Chilean Journal of Statistics and serves as an editor for several high-profile international journals. For more information, please visit his website: www.victorleiva.cl.

Viviana Giampaoli received her Ph.D. in Statistics from the University of São Paulo in 1999. From 1991 to 2001, she was a faculty member at the National University of Córdoba, and from 2001 to 2004 at the Federal University of Pernambuco. Since 2005, she has been with the Department of Statistics at the Institute of Mathematics and Statistics, University of São Paulo, where she has held the position of Associate Professor since 2022. She held the position of President of the Brazilian Statistical Association from 2022 to 2024. Her academic activities include the supervision of master's and doctoral students, as well as publications focused on the application of statistical methods to data analysis in multiple domains. Her primary research interests are in parametric inference, with a focus on mixed regression models and prediction methods.

Diana Prieto is an Assistant Professor of Industrial Engineering at Pontificia Universidad Católica de Valparaíso (PUCV), Chile, and Courtesy Assistant Professor of Operations Management and Data Analytics at Johns Hopkins Carey Business School, United States (U.S.) Diana Prieto holds a Ph.D. in Industrial Engineering and an M.A. in Statistics from the University of South Florida. Her research focuses on public health systems, decision modeling, and healthcare operations, with an emphasis on improving population health outcomes through advanced analytics. Dr. Prieto has published extensively in peer-reviewed journals, covering topics such as epidemic forecasting, healthcare disparities, and disease surveillance systems. She has led and contributed to interdisciplinary research projects funded by organizations including the U.S. National Science Foundation, Johns Hopkins University, and PUCV. With over a decade of academic experience in both the U.S. and Latin America, Dr. Prieto has taught graduate and undergraduate courses in operations research, data analytics, and health systems engineering. Dr. Prieto's work bridges academia and practice, and she frequently engages in quality improvement initiatives and collaborative partnerships with public health and governmental institutions, hospitals, and NGOs.

Carlos Martin-Barreiro — Assistant Professor of Mathematics and Computer Science at Escuela Superior Politécnica del Litoral, Ecuador Carlos Martin-Barreiro received the PhD degree from the University of Salamanca, Spain. He is currently a Assistant Professor of Mathematics and Computer Science at Escuela Superior Politécnica del Litoral, Guayaquil, Ecuador, with more than 20 years of academic experience. He has also been a software developer for public and private sector companies for more than 25 years. His current interests include the design and implementation of numerical methods for statistics and optimization.

Johanna Viana is a medical doctor specializing in nephrology, currently practicing in Braga and Guimarães, Portugal She holds a master's degree in medicine from the School of Medicine at the University of Minho (2020), Portugal. She has actively participated in conferences, seminars, and various training courses, and has contributed as both first author and co-author to numerous poster presentations and publications in national and international forums on nephrology and internal medicine. Johanna is committed to continuous professional development and strongly advocates a multidisciplinary approach to patient care.