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# Factors associated with mortality among patients aged 12 years and above requiring hospitalization for severe respiratory illness (SRI): Findings from the COVID-19 vaccine effectiveness evaluation in Kenya and Mali, 2022–2023

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ABSTRACT

*Background:* Mortality attributed to respiratory illnesses is well characterized in children <5 years. However, there is paucity of data among older populations. Here, we leveraged data from the COVID-19 Vaccine Effectiveness Evaluation to establish the factors associated with mortality among patients with severe respiratory illness (SRI) in Kenya and Mali.

*Methods:* We enrolled patients (≥ 12 years) requiring hospitalization for SRI, defined as acute onset (≤ 14 days) of at least two of the following: cough, fever (reported/measured temperature of ≥38 °C), chills, rigors, myalgia, headache, sore throat, fatigue, congestion or runny nose, loss of taste or smell, or pneumonia diagnosis, from referral hospitals in Kenya and Mali. We collected demographic, clinical characteristics of the patients, and nasopharyngeal and oropharyngeal specimens for SARS-CoV-2 testing using RT-PCR. A mixed-effects logistic regression model was fitted to identify factors associated with 30-day mortality among patients with SRI.

*Results:* Between July 2022 and October 2023 9947 SRI patients were enrolled, of whom 9743 were included in this analysis and 1620 (16.6 %) died (Kenya: 1533/7822 [20.0 %]; Mali: 87/1921 [4.5 %]). Compared to patients aged 12–24 years, those aged >64 years were more likely to die (adjusted Odds Ratio [aOR] = 2.36; 95 %

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Confidence Interval [95 % CI] 1.72–3.24). Patients who were in coma (aOR = 3.45; 95 %CI 2.27–5.24) or Intensive Care Unit (aOR = 2.98; 95 %CI 2.06–4.31), or had HIV infection (aOR = 2.47; 95 %CI 2.11–2.90), liver disease (aOR = 2.42; 95 %CI 1.57–3.74), cancer (aOR = 2.09; 95 %CI 1.46–2.99) or SARS-CoV-2 infected (aOR = 1.24; 95 %CI 1.02–1.52) were at increased risk of death. Additionally, diarrhea, malaise/fatigue, difficulty in breathing, confusion, mechanical ventilation, vasopressor support, malnutrition and admission to High Dependency Unit had significant associations.

*Conclusion:* Mortality was heightened among SRI patients who were older, required critical care, had chronic conditions and infected with SARS-CoV-2 suggesting need for early identification of these conditions to improve possible treatment outcomes.

## 1. Introduction

Respiratory illness causes significant morbidity and mortality globally with the greatest burden observed in low- and middle-income countries [1]. It is estimated that lower respiratory illness (LRI) caused about 369 million episodes and 2.55 million deaths in 2021 [2] while upper respiratory illness (URI) caused about 12.8 billion episodes and ~ 19,600 deaths annually [3]. Specifically, in Sub-Saharan Africa (SSA) 742,000 and 11,500 deaths are attributed to LRI and URI, respectively [2,3]. The burden of respiratory illnesses in SSA, including Kenya and Mali, is further exacerbated by various socio-economic factors, including limited access to healthcare, high rates of smoking, environmental pollution and delayed care-seeking [4].

The emergence of the SARS-CoV-2 virus in late 2019 has further complicated the landscape of respiratory illnesses by altering the epidemiology of respiratory infections and straining healthcare systems. While the morbidity and mortality attributed to respiratory illnesses is well characterized in children under 5 years old in literature including Kenya and Mali [5,6], there is paucity of data among older children and adults. Furthermore, most countries in Africa, including Mali, do not systematically collect data on outcomes of patients hospitalized with respiratory illness [7].

Understanding potential drivers of mortality among patients with severe respiratory illnesses (SRI) could inform public health interventions aimed at reducing the burden of SRI, ultimately improving health outcomes in these poor resource settings. Here, we leverage data from the COVID-19 Vaccine Effectiveness Evaluation to determine the factors associated with mortality among SRI patients between July 2022 and October 2023 in Kenya and Mali.

## 2. Methods

### 2.1. Setting and population

This project was part of a larger COVID-19 Vaccine effectiveness evaluation (CVE) conducted in Kenya and Mali by the Kenya Medical Research Institute (KEMRI) and Center for Vaccine Development of Mali (CVD-Mali) in collaboration with the respective Ministries of Health (MOH), Washington State University (WSU), US Center for Disease Control and Prevention (CDC) and World Health Organization (WHO). The target population for this evaluation was the general Kenya and Mali population seeking care for SRI from one national referral hospital and 19 county referral hospitals in Kenya and 13 sentinel health facilities in Bamako capital city (4 hospitals and 9 Referral Health centers) in Mali (Fig. 1). Recruitment in Kenya occurred between July 2022 and August 2023 while in Mali it ran between November 2022 and October 2023.

### 2.2. Design

This was a hospital-based surveillance leveraging the CVE platform. We compared SRI patients who died with those who survived within 30 days post admission in Kenya and Mali.

### 2.3. Case definitions

Severe Respiratory Illness (SRI) was defined as a patient who was hospitalized or recommended for hospitalization by a clinician and had acute respiratory illness (onset ≤14 days) of at least two of the following: cough, fever (reported or measured temperature of ≥38 °C), chills, rigors, myalgia, headache, sore throat, fatigue, congestion or runny nose, loss of taste or smell, OR pneumonia based on clinical diagnosis or x-ray. Cases were defined as SRI patient aged ≥12 years

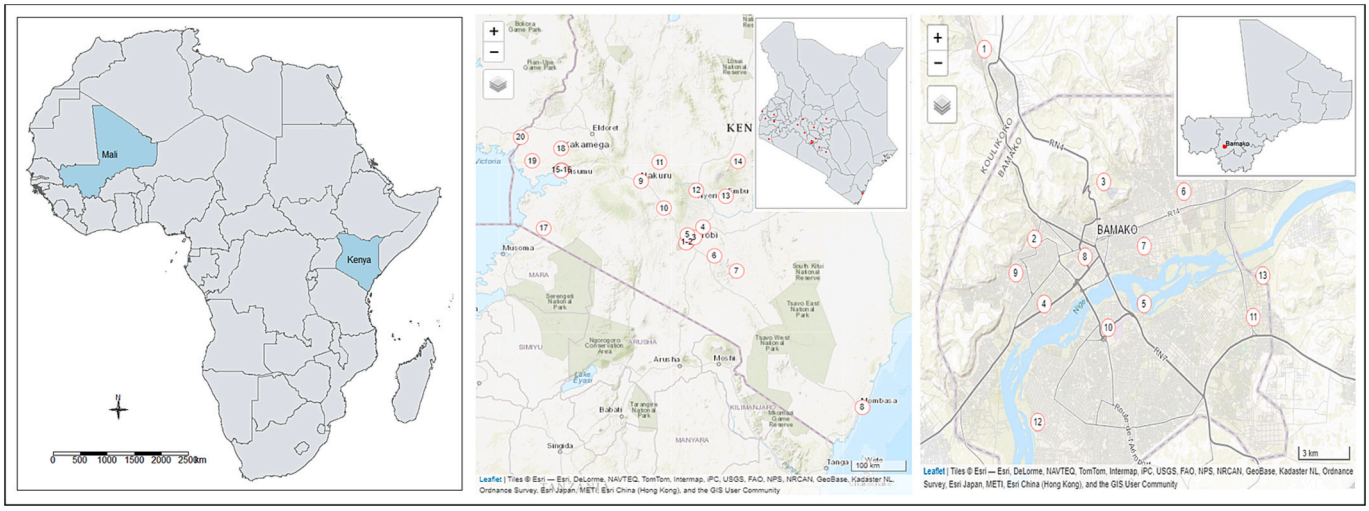


**Fig. 1.** Map showing the COVID-19 Vaccine Effectiveness Evaluation sites in Kenya and Mali.

who died within 30 days post admission while survivors were defined as those whose health status was confirmed as alive 30 days post admission. Periodic supportive supervisory visits were conducted across the sites in Kenya to oversee the implementation of recruitment, clinical, laboratory and data collection procedures as outlined in the protocol.

### 2.4. Data collection

Trained clinical officers screened patients seeking care for SRI at out/in patient and special clinics within the sentinel facilities. Those who met SRI case definition and provided written informed consent were subsequently enrolled. Socio-demographic and clinical information were collected using a standardized questionnaire programed in a window surface Go2 tablets. Patient illness records and outcome data were abstracted from patient files or electronic medical records at discharge. Data were transmitted daily via a Virtual Private Network (VPN) provided by selected service providers in Kenya and Mali to a secure, password-protected central database hosted on servers located at the KEMRI and CVD offices in Kisumu, Kenya, and Bamako, Mali, respectively. We also conducted 30-day follow up either by structured phone call interviews for those discharged or in-person assessment for those who were still hospitalized to assess their health status. Routine data quality assessment was conducted by the study statistician.

### 2.5. Specimen collection and testing.

Nasopharyngeal (NP) and oropharyngeal (OP) specimens were collected within 48hours of presentation/admission from participants according to the US CDC guidelines for collecting and Handling of clinical specimens for COVID-19 testing [8]. In brief, NP swabs were collected using a fine tipped polyester aluminum shaft swab while OP swabs were collected using a Dacron plastic shaft swab. For each patient, both swabs were placed in a single cryovial with viral transport media (VTM) and refrigerated or stored in cool boxes at temperatures ranging from 2 to 8 °C then transported to the KEMRI or CVD laboratories in Kenya and Mali, respectively where they were frozen immediately at -80 °C until testing as described elsewhere [8] or tested for SARS-CoV-2 by RT-PCR and then aliquoted and stored at -80 °C.

### 2.6. Statistical analysis

Counts and percentages, mean and standard deviation, median and range were used to summarize the data. Pearson's chi square was used to compare categorical demographic and clinical variables, whereas student's *t*-test and Wilcoxon rank sum tests were used in comparing continuous variables depending on their distribution. Fisher's exact was used to compare categorical variables where expected values were less than five. We plotted Kaplan-Meier Survival curve between SRI patients aged ≤64 years and those aged >64 years. Before adjustment, the collinearity of independent categorical variables was checked using V Cramer's statistic method and the variable with less improvement on the adjusted model dropped. Sensitivity analysis was done for both countries. A mixed-effects logistic regression model was fitted to identify factors associated with 30-day mortality among patients with SRI. The mixed-effect model accounted for clustering in space (site) and time (month of illness onset). Age, sex, and SARS-CoV-2 infection were included in the model as priori based on established evidence of their association with respiratory diseases and mortality [9] [10] [11] [12]. Additionally, all significant variables at $p < 0.2$ in the bivariate analysis were included in the multivariable model. Statistical significance was considered when *p*-value was <0.05. All the statistical analyses were conducted using R v 4.4.1 (R Core Team, Vienna, Austria).

### 2.7. Ethical considerations

The current study was part of CVE protocol which was reviewed and approved by the KEMRI Scientific and Ethics Review Unit (KEMRI SERU #-4433), the US CDC, and WHO (Protocol ID: AFR/ERC/2021/5.3.), as well as the Ethics Committee of Faculty of Medicine and Odonto-Stomatology (FMOS) in Mali (#4433). Reliance was also obtained from the Washington State University Institutional Review Board (WSU IRB). All sentinel health facilities provided administrative approval for the protocol before implementation. Written informed consent was obtained from each participant, next of kin or caretaker before their participation.

## 3. Results

### 3.1. Patient characteristics

Between July 2022 to October 2023 a total of 9947 patients requiring hospitalization for SRI were enrolled for the CVE study. The current study included 9743 patients who had complete follow up data; 7822 and 1921 participants from Kenya and Mali respectively (Fig. 2). Of these, 8522 (87.5 %) were hospitalized. The median age in years was 45 [Interquartile range-IQR: 45 [31–64] with most being >64 years from both countries. Patients from Kenya were significantly older than Mali, [IQR]: 46 [32–65] vs 41 [28–60], $p < 0.01$ with majority being males (53.2 %). Overall, there were 1620 (16.6 %) deaths, with Kenya having a significantly higher mortality rate compared to Mali (1533, [19.6 %] vs 87 [4.5 %], $p < 0.01$). Post-discharge mortality related to index SRI episode as reported at 30-day follow-up was 107/1533 (7.0 %) and 0/87 (0 %) in Kenya and Mali, respectively **(**Table 1**).**

The Kaplan-Meier survival curves compare the survival probability over time (in days) between two groups of individuals ≤64 years vs individuals >64 years (**Fig. S1**). Individuals aged >64 years had a lower probability of survival throughout the 30 day period compared to those aged ≤64 years. Additionally, individuals aged >64 years had a shorter median survival time compared to those aged ≤64 years (10 vs 11 days, $p < 0.001$).

### 3.2. Factors associated with mortality

From the bivariate model, the SRI patients who died were significantly older than those who survived (median age in years [IQR]: 53 [38–71] vs 43 [30–62], $p < 0.01$) and were more likely to be male (917 [55.6 %]). Those who died sought care later (median days [IQR]: 5

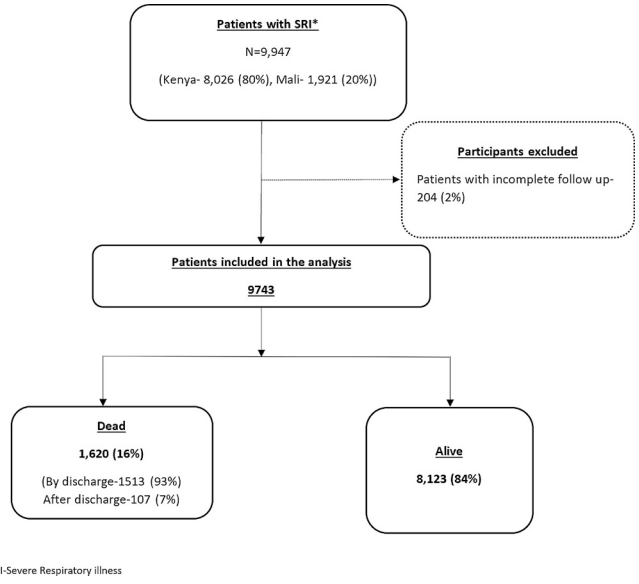


**Fig. 2.** Enrolment flowchart of mortality among patients presenting with severe respiratory illness in Kenya and Mali, July 2022 to October,2023.

**Table 1**
Characteristics of patients recommended for hospitalization with severe respiratory illness in Kenya and Mali, July 2022–October 2023.

| Demographic characteristics | All participants, *n* = 9743 | Kenya- *n* = 7822 | Mali- *n* = 1921 | *p*-value |
|---|---|---|---|---|
| | **n (%)** | **n (%)** | **n (%)** | |
| **Age (in years)** | | | | |
| Median (IQR) | 45 [31–64] | 46 [32–65] | 41 [28–60] | **<0.01** |
| **Age category** | | | | |
| 12—24 | 1344 (13.8) | 1012 (12.9) | 332 (17.3) | **<0.01** |
| 25–34 | 1673 (17.2) | 1256 (16.1) | 417 (21.7) | |
| 35–44 | 1798 (18.5) | 1492 (19.1) | 306 (15.9) | |
| 45–54 | 1380 (14.2) | 1113 (14.2) | 267 (13.9) | |
| 55–64 | 1164 (11.9) | 915 (11.7) | 249 (13.0) | |
| >64 | 2384 (24.5) | 2034 (26.0) | 350 (18.2) | |
| **Gender,** male | 4936 (50.7) | 4165 (53.2) | 771 (40.1) | **<0.01** |
| **Occupation** | | | | |
| Formal employment | 1054 (10.8) | 766 (9.8) | 288 (15.0) | **<0.01** |
| Self-employment | 2939 (30.2) | 2612 (33.4) | 327 (17.0) | |
| Not employed | 3943 (40.5) | 3790 (48.5) | 153 (8.0) | |
| Students | 918 (9.4) | 654 (8.4) | 264 (13.7) | |
| Part-time employment | 83 (0.9) | 0 (0.0) | 83 (4.3) | |
| Others | 806 (8.3) | 0 (0.0) | 806 (42.0) | |
| **Hospitalization status** | | | | |
| Recommended-not hospitalized | 1221 (12.5) | 1221 (15.6) | 0 (0.0) | **<0.01** |
| Recommended and hospitalized | 8522 (87.5) | 6601 (84.4) | 1921 (100.0) | |
| **Outcome** | | | | |
| Alive | 8123 (83.4) | 6289 (80.4) | 1834 (95.5) | **<0.01** |
| Dead | 1620 (16.6) | 1533 (19.6) | 87 (4.5) | |

**Table 2**
Characteristics of enrolled patients among those who died or survived, July 2022-Oct 2023.

| Characteristics | All participants, n = 9743 | Died- *n* = 1620 | Alive- *n* = 8123 | p-value |
|---|---|---|---|---|
| | n (%) | n (%) | n (%) | |
| **Age (in years)** | | | | |
| Median (IQR) | 45 [31–64] | 53 [38–71] | 43 [30–62] | **<0.01** |
| **Age category** | | | | |
| 12–24 | 1344 (13.8) | 102 (6.3) | 1242 (15.3) | **<0.01** |
| 25–34 | 1673 (17.2) | 196 (12.1) | 1477 (18.2) | |
| 35–44 | 1798 (18.5) | 304 (18.8) | 1494 (18.4) | |
| 45–54 | 1380 (14.2) | 233 (14.4) | 1147 (14.1) | |
| 55–64 | 1164 (11.9) | 204 (12.6) | 960 (11.8) | |
| >64 | 2384 (24.5) | 581 (35.9) | 1803 (22.2) | |
| **Gender,** male | 4936 (50.7) | 917 (56.6) | 4019 (49.5) | **<0.01** |
| **Occupation** | | | | |
| Formal employment | 1054 (10.8) | 108 (6.7) | 946 (11.6) | **<0.01** |
| Self-employment | 2939 (30.2) | 448 (27.7) | 2491 (30.7) | |
| Not employed | 3943 (40.5) | 958 (59.1) | 2985 (36.7) | |
| Students | 918 (9.4) | 60 (3.7) | 858 (10.6) | |
| Part-time employment | 83 (0.9) | 3 (0.2) | 80 (1.0) | |
| Others | 806 (8.3) | 43 (2.7) | 763 (9.4) | |
| **Vitals** | | | | |
| Respiratory rate (>20), *n* = 9736 | 5365 (55.1) | 1066 (65.9) | 4299 (53.0) | **<0.01** |
| Oxygen saturation (<90), *n* = 9708 | 2146 (22.1) | 627 (38.9) | 1519 (18.8) | **<0.01** |
| **Clinical symptoms** | | | | |
| Headache, *n* = 9735 | 5517 (56.7) | 626 (38.7) | 4891 (60.3) | **<0.01** |
| Fever, *n* = 9703 | 3701 (38.1) | 453 (28.2) | 3248 (40.1) | **<0.01** |
| Cough, *n* = 9741 | 8196 (84.1) | 1388 (85.7) | 6808 (83.8) | 0.07 |
| Chills, *n* = 9738 | 3796 (39) | 458 (28.3) | 3338 (41.1) | **<0.01** |
| Rigors, *n* = 9727 | 1009 (10.4) | 157 (9.7) | 852 (10.5) | 0.36 |
| Sore throat, *n* = 9740 | 1938 (19.9) | 152 (9.4) | 1786 (22.0) | **<0.01** |
| Diarrhea, *n* = 9711 | 809 (8.3) | 187 (11.6) | 622 (7.7) | **<0.01** |
| Vomiting, *n* = 9732 | 1549 (15.9) | 294 (18.2) | 1255 (15.5) | **0.01** |
| Sore muscles, *n* = 9719 | 3190 (32.8) | 381 (23.7) | 2809 (34.6) | **<0.01** |
| Fatigue/ Malaise, n = 9741 | 6975 (71.6) | 1184 (73.1) | 5791 (71.3) | 0.16 |
| Nasal Congestion, *n* = 9742 | 1609 (16.5) | 200 (12.3) | 1409 (17.3) | **<0.01** |
| Runny nose, *n* = 9731 | 1956 (20.1) | 127 (7.9) | 1829 (22.5) | **<0.01** |
| Loss of taste/ smell, n = 9738 | 2095 (21.5) | 248 (15.3) | 1847 (22.7) | **<0.01** |
| Abnormal breath sounds, *n* = 9723 | 4409 (45.3) | 829 (51.2) | 3580 (44.2) | **<0.01** |
| Difficulty in breathing, n = 9740 | 5813 (59.7) | 1263 (78.0) | 4550 (56.0) | **<0.01** |
| Skin rash, n = 9731 | 175 (1.8) | 33 (2.0) | 142 (1.8) | 0.49 |
| Conjunctivitis, *n* = 9734 | 153 (1.6) | 19 (1.2) | 134 (1.7) | 0.19 |
| Convulsions, *n* = 9728 | 254 (2.6) | 55 (3.4) | 199 (2.5) | **0.04** |
| Irritability, *n* = 9716 | 768 (7.9) | 266 (16.5) | 502 (6.2) | **<0.01** |

(*continued on next page*)

[2–7] vs 4 [2–7], p < 0.01). Clinical symptoms including, diarrhea, vomiting, abnormal breath sounds, difficulty in breathing, irritability and coma were positively associated with death while those presenting with headache, fever, chills, sore throat, sore muscles, nasal congestion, runny nose, loss of taste, new loss of taste, new loss of smell, ear pain discharge, pharyngeal exudate had a negative association with death (Table 2). Additionally, patients who required mechanical ventilation or vasopressor support as well as those who were in intensive care unit or high dependence unit were more likely to die. Comorbidities and chronic conditions including HIV, neuromuscular disease, tuberculosis (TB), heart disease, malnutrition, liver disease, hypertension and cancer-related conditions were positively associated with mortality. Chronic conditions were more prevalent in older patients presenting with SRI.

SARS-CoV-2 was also positively associated with death at bivariate analysis level (Table 2).

From the multivariable model, the odds of mortality increased with age and was highest among those aged >64 years (adjusted Odds Ratio -aOR [95 % Confidences interval- 95 % CI]: 2.36 [1.72–3.24]). Additionally, male SRI patients had increased odds of death (aOR [95 % CI]: 1.18 [1.03–1.34]). Patients who had diarrhea (aOR [95 % CI]: 1.75 [1.42–2.16), difficulty in breathing (aOR [95 % CI]: 1.58 [1.33–1.86]), malaise/fatigue (aOR [95 % CI]: 1.36 [1.16–1.60]), had abnormal breath sounds (aOR [95 % CI]: 1.24 [1.06–1.45])irritability/confusion

**Table 2** (*continued*)

| Characteristics | All participants, n = 9743 | Died- *n* = 1620 | Alive- *n* = 8123 | p-value |
|---|---|---|---|---|
| | n (%) | n (%) | n (%) | |
| Abdominal pain, n = 9728 | 1425 (14.6) | 252 (15.6) | 1173 (14.5) | 0.25 |
| Pharyngeal exudate, *n* = 9726 | 1152 (11.8) | 118 (7.3) | 1034 (12.7) | **<0.01** |
| Coma, n = 9723 | 149 (1.5) | 73 (4.5) | 76 (0.9) | **<0.01** |
| **Patient management** | | | | |
| ICU, n = 9743 | 481 (4.9) | 165 (10.2) | 316 (3.9) | **<0.01** |
| High dependence unit, n = 9743 | 171 (1.8) | 77 (4.8) | 94 (1.2) | **<0.01** |
| Mechanical ventilation, *n* = 9743 | 522 (5.4) | 279 (17.2) | 243 (3.0) | **<0.01** |
| Vasopressor support, n = 9743 | 225 (2.3) | 112 (6.9) | 113 (1.4) | **<0.01** |
| **Chronic conditions** | | | | |
| HIV, *n* = 9691 | 1534 (15.8) | 452 (27.9) | 1082 (13.4) | **<0.01** |
| Neuromuscular disease, *n* = 9729 | 166 (1.7) | 45 (2.8) | 121 (1.5) | **<0.01** |
| TB, n = 9743 | 796 (8.2) | 195 (12.0) | 601 (7.4) | **<0.01** |
| Heart disease, *n* = 9717 | 720 (7.4) | 188 (11.6) | 532 (6.6) | **<0.01** |
| Malnutrition, n = 9743 | 246 (2.5) | 81 (5.0) | 165 (2) | **<0.01** |
| Liver disease, *n* = 9724 | 123 (1.3) | 45 (2.8) | 78 (1.0) | **<0.01** |
| Diabetes, n = 9743 | 865 (8.9) | 153 (9.4) | 712 (8.8) | 0.41 |
| Hypertension, n = 9743 | 2001 (20.5) | 367 (22.7) | 1634 (20.1) | **0.02** |
| Asthma, n = 9743 | 510 (5.2) | 40 (2.5) | 470 (5.8) | **<0.01** |
| Cancer, *n* = 9714 | 186 (1.9) | 66 (4.1) | 120 (1.5) | **<0.01** |
| Sickle cell disease, n = 9726 | 75 (0.8) | 6 (0.4) | 69 (0.9) | 0.06 |
| **Median days to seeking care, (IQR)** | 4 [2–7] | 5 [2–7] | 4 [2–7] | **<0.01** |
| **Days to seek care from onset** | | | | |
| 1–3 | 4030 (41.4) | 645 (39.8) | 3385 (41.7) | |
| 4–7 | 3677 (37.7) | 591 (36.5) | 3086 (38.0) | |
| **>7** | 2036 (20.9) | 384 (23.7) | 1652 (20.3) | **<0.01** |
| **SARS-CoV-2 test** | | | | |
| Positive, n = 9732 | 579 (5.9) | 127 (7.8) | 452 (5.6) | **<0.01** |

(aOR [95 % CI]: 2.43 [1.99–2.96]), were in a coma (aOR [95 % CI]: 3.45 [2.27–5.24]), required mechanical ventilation (aOR [95 % CI]: 5.57 [4.30–7.21]) or vasopressor support (aOR [95 % CI]: 4.26 [2.91–6.23]), or were admitted to ICU (aOR [95 % CI]: 2.98 [2.06–4.31]) or HDU (aOR [95 % CI]: 1.92 [1.28–2.89]) were at increased odds of death. Moreover, those who had chronic conditions or comorbidities (HIV (aOR [95 % CI]: 2.47 [2.11–2.90]), neuromuscular disease (aOR [95 % CI]: 1.71 [1.10–2.66]), malnutrition (aOR [95 % CI]: 1.76 [1.27–2.44]), liver disease (aOR [95 % CI]: 2.42 [1.57–3.74]) and cancer (aOR [95 % CI]: 2.09 [1.46–2.99]) had increased odds of death. On the contrary, SRI patients presenting with headache (aOR [95 % CI]: 0.70 [0.61–0.81], $p < 0.01$), runny nose (aOR [95 % CI]: 0.64 [0.51–0.81]), sore throat (aOR [95 % CI]: 0.70 [0.56–0.88]), and sore muscles (aOR [95 % CI]: 0.81 [0.68–0.97]) had reduced odds of mortality (Table 3). The site-stratified analysis is shown in Table S1. Additionally, the analysis stratified by chronic conditions are shown in Table S2.

Furthermore, when we assessed the number of underlying conditions an individual had, the odds of death increased with an increase in the number of underlying conditions. Individuals with one underlying condition had higher odds compared to those with no underlying condition (OR = 1.72, [1.51–1.95]). This risk increased as the number of conditions increased with patients having ≥4 conditions having the highest odds of mortality compared to the reference group (OR = 2.99, [1.61–5.33]).

**Table 3**
Factors associated with mortality among patients enrolled with severe respiratory illness in Kenya and Mali, July 2022–October 2023.

| Characteristics | OR (95 %CI) | aOR (95 % CI) * | p-value |
|---|---|---|---|
| **Age category** | | | |
| 12–24 | **Ref** | | |
| 25–34 | **1.62 [1.26–2.08]** | 1.26 [0.90–1.76] | 0.17 |
| 35–44 | **2.48 [1.96–3.14]** | **1.50 [1.08–2.09]** | **0.01** |
| 45–54 | **2.47 [1.93–3.16]** | **1.62 [1.16–2.27]** | **<0.01** |
| 55–64 | **2.59 [2.01–3.33]** | **1.82 [1.29–2.55]** | **<0.01** |
| >64 | **3.92 [3.14–4.90]** | **2.36 [1.72–3.24]** | **<0.01** |
| **Gender-** male | **1.33 [1.20–1.48]** | **1.18 [1.03–1.34]** | **0.01** |
| **Occupation** | | | |
| Formal employment | **Ref** | **Ref** | |
| Self-employment | **1.58 [1.26–1.97]** | 1.01 [0.78–1.32] | 0.93 |
| Not employed | **2.81 [2.27–3.47]** | **1.38 [1.06–1.81]** | **0.02** |
| Students | **0.61 [0.44–0.85]** | 1.05 [0.68–1.63] | 0.83 |
| Part-time employment | 0.33 [0.10–1.06] | 0.33 [0.07–1.63] | 0.17 |
| Others | **0.49 [0.34–0.71]** | 0.93 [0.55–1.56] | 0.78 |
| **Vitals** | | | |
| Respiratory rate (>20) | **1.72 [1.53–1.92]** | 1.07 [0.92–1.24] | 0.39 |
| Oxygen saturation (<90) | **2.75 [2.45–3.09]** | **1.48 [1.27–1.72]** | **<0.01** |
| **Clinical symptoms** | | | |
| Headache | **0.42 [0.37–0.46]** | **0.70 [0.61–0.81]** | **<0.01** |
| Fever | **0.58 [0.52–0.66]** | | |
| Cough | 1.15 [0.99–1.34] | | |
| Chills | **0.57 [0.50–0.64]** | | |
| Rigors | 0.92 [0.77–1.10] | | |
| Sore throat | **0.37 [0.31–0.44]** | **0.70 [0.56–0.88]** | **<0.01** |
| Diarrhea | **1.58 [1.33–1.88]** | **1.75 [1.42–2.16]** | **<0.01** |
| Vomiting | **1.21 [1.05–1.39]** | **1.21 [1.01–1.45]** | **0.04** |
| Sore muscles | **0.59 [0.52–0.66]** | **0.81 [0.68–0.97]** | **0.02** |
| Fatigue/ Malaise | 1.09 [0.97–1.23] | **1.36 [1.16–1.60]** | **<0.01** |
| Nasal Congestion | **0.67 [0.57–0.79]** | | |
| Runny nose | **0.29 [0.24–0.35]** | **0.64 [0.51–0.81]** | **<0.01** |
| Loss of taste/smell | **0.62 [0.53–0.71]** | | |
| Abnormal breath sounds | **1.33 [1.19–1.48]** | **1.24 [1.06–1.45]** | **0.01** |
| Difficulty in breathing | **2.78 [2.45–3.15]** | **1.58 [1.33–1.86]** | **<0.01** |
| Skin rash | 1.17 [0.80–1.71] | | |
| Conjunctivitis | 0.71 [0.44–1.15] | | |
| Convulsions | **1.40 [1.03–1.90]** | | |
| Irritability/ confusion | **2.98 [2.54–3.49]** | **2.43 [1.99–2.96]** | **<0.01** |
| Abdominal pain | 1.09 [0.94–1.27] | | |
| Pharyngeal exudate | 0.54 [0.44–0.66] | | |
| Coma | **5.00 [3.61–6.92]** | **3.45 [2.27–5.24]** | **<0.01** |
| **Patient management** | | | |
| ICU | **2.80 [2.30–3.41]** | **2.98 [2.06–4.31]** | **<0.01** |
| High dependence unit | **4.26 [3.14–5.79]** | **1.92 [1.28–2.89]** | **<0.01** |
| Mechanical ventilation | **6.75 [5.63–8.09]** | **5.57 [4.30–7.21]** | **<0.01** |
| Vasopressor support | **5.26 [4.03–6.88]** | **4.26 [2.91–6.23]** | **<0.01** |
| **Chronic conditions** | | | |
| HIV | **2.52 [2.22–2.86]** | **2.47 [2.11–2.90]** | **<0.01** |
| Neuromuscular disease | **1.89 [1.34–2.68]** | **1.71 [1.10–2.66]** | **0.02** |
| TB | **1.71 [1.44–2.03]** | 1.16 [0.94–1.43] | 0.18 |
| Heart disease | **1.87 [1.57–2.23]** | 1.18 [0.96–1.46] | 0.12 |
| Malnutrition | **2.54 [1.93–3.33]** | **1.76 [1.27–2.44]** | **<0.01** |
| Liver disease | **2.95 [2.04–4.27]** | **2.42 [1.57–3.74]** | **<0.01** |
| Diabetes | 1.09 [0.90–1.30] | | |
| Hypertension | **1.16 [1.02–1.32]** | | |
| Asthma | **0.41 [0.30–0.57]** | **0.36 [0.25–0.51]** | **<0.01** |
| Cancer | **2.83 [2.08–3.84]** | **2.09 [1.46–2.99]** | **<0.01** |
| Sickle cell disease | 0.43 [0.19–1.00] | 0.72 [0.27–1.92] | 0.51 |
| **Time to seek care (IQR)** | | | |
| 1–3 | **Ref** | | |
| 4–7 | 1.01 [0.89–1.14] | 1.01 [0.87–1.18] | 0.85 |
| **>7** | **1.22 [1.06–1.40]** | 1.08 [0.91–1.28] | 0.40 |
| **SARS-CoV-2 test** | | | |
| Positive | **1.44 [1.18–1.77]** | **1.24 [1.02–1.52]** | **0.03** |

*Adjusted for Age- Site- Sex- and variables significant at $p = 0.2$

### 3.3. SARS-CoV-2 and mortality positivity

The period between July and December 2022 was marked with the highest mortality and *SARS-CoV-2 positivity*. In 2023, the early months

are marked with a period of waves and later the mortality and *SARS-CoV-2* trend dropped (Fig. 3).

## 4. Discussion

We assessed the factors associated with mortality among SRI patients leveraging the CVE evaluation in Kenya and Mali. Key findings from our study included: i.) SRI patients aged ≥35 was associated with higher risk of death with this differential peaking among those aged >64 ii.) Critically ill SRI patients including those presenting with coma, confusion, diarrhea, difficulty in breathing, fatigue and vomiting as well as those who required critical care were more likely to die iii.) SRI patients with chronic conditions that included HIV, liver disease, cancer-related conditions, malnutrition or neuromuscular disease had an elevated risk of mortality iv.) Finally, mortality was significantly higher among SRI patients who tested positive for SARS-CoV-2.

Our observation that mortality increased with age is congruent with findings from the global burden of disease showing that age standardized death rates were highest in adults aged 70 and above [13]. Our findings are consistent with other observations from SSA showing increased mortality in the elderly population [14]. This finding can be explained by waning immunity as well as age-related pathophysiological and anatomical changes in the elderly, which reduces their ability to fight infections as further demonstrated elsewhere [15]. In addition, older age group has been reported as a hindrance to prompt care-seeking in SSA potentially leading to presentation with severe disease that predisposes them to adverse health outcomes including mortality [16]. This finding underscores the importance of creating awareness on timely care-seeking among this age group, prioritizing them in preventive strategies as well as giving them urgent medical attention when they seek care.

We also observed that critically ill SRI patients including those presenting with coma, confusion, diarrhea, difficulty in breathing, fatigue and vomiting as well as those who required critical care such as mechanical ventilation, vasopressor support or intensive care units were more likely to die. Some of these symptoms and the need for critical care represent severe manifestation of disease that are likely related to delay in seeking care as further demonstrated in our data. Furthermore, these observations aligns with existing literature showing that patients requiring critical care have worse hospital outcomes, particularly death [17–19]. This finding could possibly be due to complications arising from delay in seeking care as also observed in our current study heightened severity of illness which could explain the increased need of critical care among SRI patients who died. Furthermore, late care-seeking is a common problem in LMICs including the study settings [20] and most patients would seek care when the illness has advanced leading to poor health outcomes. Consequently, interventions targeted at reducing mortality due to SRI should take into account delayed care-seeking and improved healthcare system, especially during pandemic situations.

In our current study, mortality was significantly pronounced among SRI patients with chronic conditions that included HIV, liver disease, cancer-related conditions, malnutrition or neuromuscular disease. These findings are not dissimilar to other observations from existing literature [21–24], suggesting that chronic conditions have the potential to weaken the immune system and impairs the body's ability to combat infections and increases susceptibility to complications. Additionally, patients with chronic conditions require comprehensive management that could lead to challenges in providing effective care, potentially increasing the risk of death. Moreover, this could be worse in situation of health emergencies like during the study period when there was a strain on health system, which leads to suboptimal service delivery in resource limited settings such as Kenya and Mali. These observations suggest that optimizing care and creating awareness on chronic conditions and their effect on primary infections such as severe respiratory illness is crucial.

Finally, mortality was significantly higher among SRI patients who tested positive for SARS-CoV-2 consistent with previous studies [25,26]. This increased risk may be due to the severe complications associated with SARS-CoV-2 infections, such as acute respiratory distress syndrome (ARDS), multi-organ failure, and exacerbation of existing health conditions [27]. Additionally, the virus's impact on the immune system and its potential to trigger severe inflammatory responses contribute

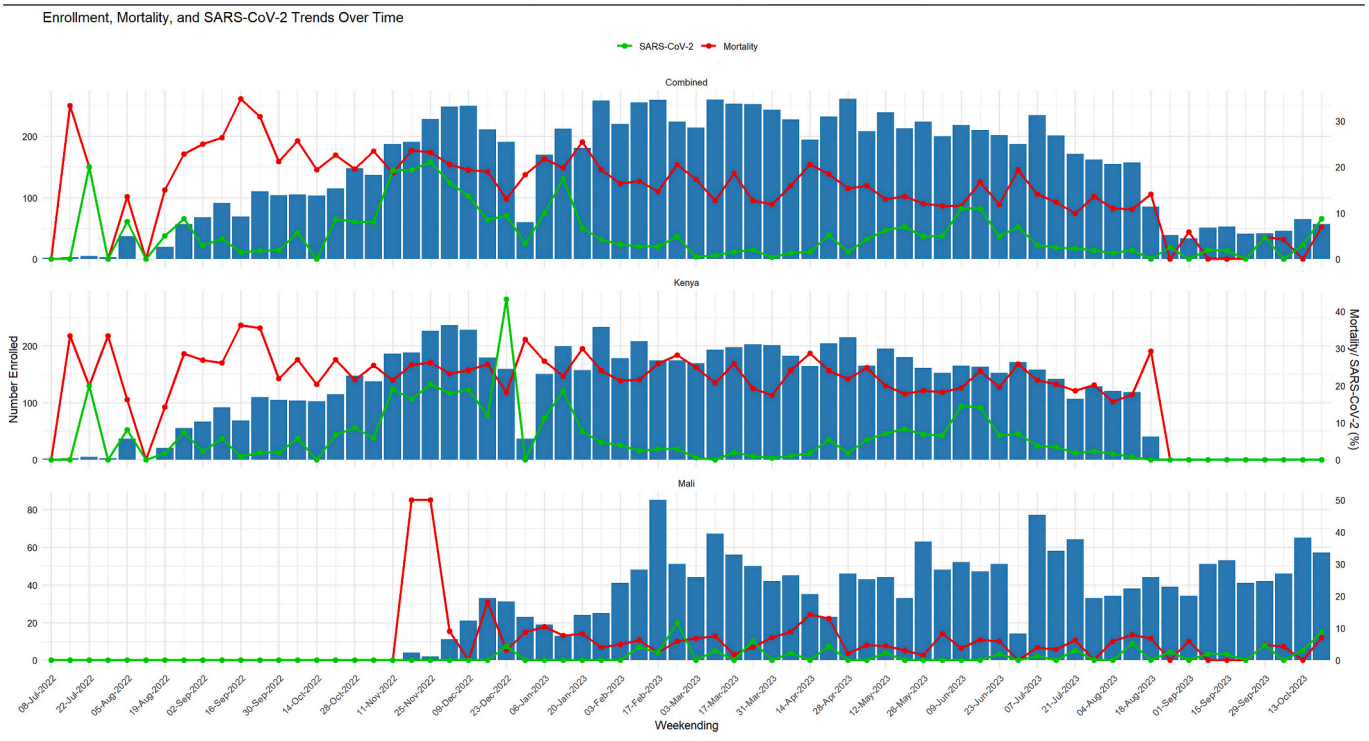


**Fig. 3.** Trends of mortality among patients presenting with severe respiratory illness in Kenya and Mali July 2022 to October,2023.

significantly to the increased mortality observed in these patients. Public health strategies should prioritize COVID-19 preventive strategies as well as expanding testing and early detection for timely intervention and containment.

Taken together, the above findings highlight the need to prioritize high-risk groups, including the elderly and those with chronic conditions, for vaccination and timely clinical management. Additionally, healthcare systems need enhanced capacity, including ICU beds, ventilators, and trained personnel to manage severe SRI cases. There is also need for ongoing public health awareness on prompt care-seeking, chronic conditions and preventive and curative interventions for SRI patients. Future research should explore the role of COVID-19 vaccination in mitigating mortality risk, particularly among high-risk individuals. Additionally, studies assessing the impact of healthcare access, early treatment initiation, and post-hospitalization outcomes could provide a more comprehensive understanding of mortality drivers in resource-limited settings.

While our findings on factors associated with mortality among patients with SRI are important, this study was not without limitations. First, our study may have underestimated the mortality as it was hospital-based study conducted in settings with known challenges in healthcare access and delayed care-seeking behavior. This may have led to the exclusion of individuals who died before reaching the hospital or sought care at non-participating facilities. Secondly, there was limited data on etiologies of SRI with testing only done for SARS-CoV-2. Finally, our study was not originally powered for mortality. However, the sample size was large enough to ascertain the differences.

## 5. Conclusion

Mortality was heightened among SRI patients who were older, required critical care, had chronic conditions and infected with SARS-CoV-2 suggesting need for early identification of these conditions to improve treatment outcomes.

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## Author contribution

BOO, BON, RO and SOS conceived the study. All authors contributed to study design and implementation. BOO and BON analyzed and interpreted the data. BOO drafted the manuscript and all authors critically reviewed the manuscript for intellectual content and approved the final manuscript. All authors read and approved the final manuscript.

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## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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## Data availability

Data will be made available on request.

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