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Respiratory Syncytial Virus Severity Changes in Atlanta Metropolitan Area from 2018-2022

By

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# Respiratory Syncytial Virus Severity Changes in Atlanta Metropolitan Area from 2018-2022

By

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Bachelor of Science
Mercer University
2021

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An abstract of
A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
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Abstract

Respiratory Syncytial Virus Severity Changes in Atlanta Metropolitan Area from 2018-2022

By Thomas Head

This thesis examines the severity of Respiratory Syncytial Virus (RSV) during the COVID-19 pandemic and its effects on age groups and seasonality of the virus. Data collected from the Georgia Emerging Infections Program (GEIP) from October 2018 to December 2022 was analyzed to determine changes in age-specific distribution of hospitalizations, mean length of hospital stay and mortality. Results showed that after COVID-19 restrictions were lifted, there were more hospitalizations in the summer months 2021 and 2022 than in the previous year and that the proportion of pediatric hospitalizations decreased. Additionally, mean length of stay was significantly reduced among pediatric patients, but not adults. Deaths during and after hospitalization saw non-significant changes, with pediatric and adult groups reporting non-significantly higher rates of death. The study provides a baseline for future studies to understand the changes in RSV severity on account of other major epidemics or pandemics that disrupt society's typical relationship with respiratory viruses.

# Respiratory Syncytial Virus Severity Changes in Atlanta Metropolitan Area from 2018-2022

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Table of Contents

**Background**

During the COVID-19 pandemic, incidence of other respiratory illnesses like Influenza dropped dramatically due to infection control measures such as mask usage and social distancing adopted to prevent the spread of COVID-19. One of the pathogens most affected by COVID-19 mitigation strategies was Respiratory Syncytial Virus (RSV). RSV is a highly contagious virus that causes a respiratory illness most commonly affecting children and characterized by mild flu-like symptoms, and in severe cases, substantial difficulty breathing or death[1]. Common in early childhood, RSV infects nearly all children by the age of 2 years old, with more than 50% of those less than the age of one year old being infected twice before the age of 2 years old[2,3]. RSV is the second leading cause of death among infants outside of the neonatal period, and survivors usually have recurrent infections throughout the life-course since immunity for RSV is not long-term[2,3]. RSV also has a significant burden for adults, particularly older adults 65 years or older. Key risk factors for severe RSV illness include being born prematurely, weakened immune systems, neuromuscular disorders (particularly those affecting swallowing), and chronic lung or heart diseases[2–5].

Historically, RSV is a seasonal illness with peak incidence occurring during winter months from October to April, like other respiratory diseases. It is estimated, annually, that 58,000-80,000 hospitalizations occur in children under 5 years of age resulting in 100-300 deaths[1]. Despite a relatively low fatality rate, RSV can worsen pre-existing conditions in children such as asthma, leading to further health issues later in life. In older adults it is estimated that 60,000-160,000 hospitalizations occur annually due to RSV, leading to an estimated 6,000-10,000 deaths[5–7]. In older adults, RSV causes 2-5% of all community-acquired pneumonia, increasing to 10-20% in nursing homes, with 2-5% of infections resulting in death[4].

Due to COVID-19 pandemic infection prevention measures, respiratory illnesses, including RSV, experienced disruptions in their typical epidemiology. As the pandemic began in March 2020, and mask

usage was widely used, incidence of RSV and other respiratory diseases plummeted nationally[8]. In this same period, individual infection prevention measures were supplemented with school closures and mandatory social distancing, limiting interpersonal contact. In the 2018-2019 and 2019-2020 RSV seasons, RSV hospitalization rates peaked in January, having rates of 1.8 per 100,000 and 2.7 per 100,000, respectively[9]. The 2019-2020 RSV season had a lower peak rate than any season before the COVID-19 pandemic; however, the 2022-2023 peak hospitalization rate has been nearly 2 times higher than any previous season's peak weekly hospitalization rate before the COVID-19 pandemic[9].

Georgia saw similar incidence and hospitalization trends as those observed nationally; however, historically low RSV burden continued until April 2021, notably ending when Georgia Governor, Brian Kemp, ended Georgia's statewide mask mandate on March 31, 2021. Soon after lifting the public mask mandate, the incidence of RSV increased through the Summer of 2021, prompting the Centers for Disease Control and Prevention (CDC) to declare a health advisory in June 2021. These uncharacteristic incidence increases illustrated an out of season, above-endemic level of RSV spread[10]. This trend continued through Summer 2022 and into the previously typical 2022-2023 RSV season.

The previously typical winter RSV seasons in 2021-2022 and 2022-2023 also had elevated hospitalization rates for all ages. Interestingly, there have also been unusual hospitalization rates out of season. In September 2021, the weekly peak rate for out of season hospitalizations was higher than the weekly peak rate for in-season hospitalizations[9]. Based on hospitalizations alone, Georgia has seen an increased burden of RSV in all ages after COVID-19 pandemic restrictions were lifted compared to pre-pandemic seasons. There is little research that explores the severity of RSV and how the COVID-19 pandemic may have changed the severity of RSV cases. The Georgia Emerging Infections Program (GAEIP) uses its RSV-NET Surveillance Network to conduct surveillance of hospitalizations in the state of Georgia, and using data collected data through the GAEIP, this thesis investigates the COVID-19 pandemic's role in the age distribution of RSV hospitalizations, mean length of hospital stay and mortality during a hospital stay for RSV.

## Methods

Data analyzed in this thesis comes from data collected by GAEIP, through their clinical partners in Atlanta Metropolitan area in Georgia. Through active surveillance consisting of local hospitals reporting hospitalizations, hospitalizations for a variety of diseases, including RSV, are reported to GAEIP. For the GAEIP surveillance catchment area, the case definition of a hospitalized RSV case includes the following: A resident of Cobb, Clayton, DeKalb, Douglas, Fulton, Gwinnett, Newton, Rockdale counties, admitted to the hospital 14 days or less after a positive RSV test or 3 days or less before a positive RSV test, and admitted to an inpatient ward of the hospital and/or were admitted to an observation ward and had a combined emergency department and observation time equal to or greater than 24 hours.

Data included in this analysis was obtained from October 2018 to December 2022. From this period, two time-specific stratifications were made per year of data corresponding to the traditional seasonality of RSV incidence: October to March and April to September. In addition, calendar time was divided into three categorizations: “Pre-Pandemic” (October 2018-March 2020), “Pandemic” (April 2020-March 2021), “Post-Pandemic” (April 2021-December 2022). Age group cutoffs were based on known age-based risk strata for RSV: < 6 months old, 6 months to 12 months old, and 1 year to < 2 years old, 2 to < 17 years old, 18 to 64 years old, and older than 65 years[9].

Two outcome indicators of severity were analyzed in this study: duration of stay in the hospital and death. Stay duration was assessed by calculating the mean duration of stay by age group, stratified by intensive care unit (ICU) admission and pandemic-related time period. Stratifying by ICU admission attempts to remove effect modification introduced by ICU care while stratification by proximity to the COVID-19 pandemic allows comparisons by time period. Death was determined by whether the patient was discharged alive or deceased during their hospital stay for RSV.

For analyses of mean stay differences by time periods, a two tailed T-test was used to assess mean differences at 95% confidence. Pearson's chi-square test was be used to determine significant differences in death rates by period, stratified by ICU admission. Hospital fatality rates were calculated by dividing deaths by total hospitalizations in each period, pre-pandemic (March 2018-March 2020) and post pandemic (April 2021-December 2022). The pre-pandemic time will be considered the baseline group for this study in both analyses.

No RSV data was available from April 2020-September 2020 due to GAEIP halting RSV surveillance during the height of the COVID-19 pandemic. Of all hospitalizations reported, only those that had a reported discharge date and ICU admission status (admitted or not admitted) are included in the analysis. All analyses were conducted through SAS 9.4 (Cary, NC). This study was reviewed and approved exempt by the Emory University Institutional Review Board.

**Results**

Between October 2018 and December 2022, 4,013 individuals were hospitalized with RSV. (Table 1). The median age of hospitalized individuals across the entire cohort was 1.9 years, with an interquartile range of 41.6 years. In this population, 27% of all hospitalizations self-identified as "White," and 31% self-identified as "Black or African American." Thirty-eight percent of patients did not disclose race or race was unknown. The study population was predominantly non-Hispanic, with 84% of patients self-identifying as non-Hispanic.

From October 2018 to March 2020, RSV seasonality was typical, with most hospitalizations occurring during the putative RSV season, from October 2018-March 2019 (n=720; 17.9%) and October 2019-March 2020 (n=930; 23.2%). After March 2021, there was a substantial increase in out of season hospitalizations, specifically in April 2021-September 2021 and April 2022-September 2022 (n=749 and n=778, respectively). Pediatric hospitalizations were also less frequent after March 2021, indicating a larger proportion of adult hospitalizations.

In the pre-pandemic period (October 2018 – March 2020), the age group with the highest proportion of RSV hospitalizations was children under 2 years old. They comprised 55.7% of hospitalizations from October 2018-September 2019. (Figure 1). Pediatric hospitalizations accounted for at least 74.3% and 75.9% of all hospitalizations for two out of the three pre-pandemic periods, October 2018-March 2019, and April 2019-September 2019, and 65.1% of hospitalizations for October 2019-March 2020. Infants under 6 months had the highest proportion of hospitalizations in all pre-pandemic periods, before April 2020. During the pandemic, April 2020-March 2021, 84.2% of hospitalizations were pediatric. In the 2021-2022 RSV season, hospitalizations for adults over 65 reached over 20.7%, the highest proportion seen in this age group since October 2018, while pediatric hospitalizations were at their lowest, failing to 60%. From April 2022 to September 2022, proportions were similar to pre-pandemic findings, but from October 2022 to December 2022, proportional hospitalizations for those over 65 surpassed hospitalizations for infants under 6 months for the first time since October 2018, and pediatric hospitalizations were 56.2%, the lowest percentage since October 2018.

*Pandemic impacts on length of hospital stay*

Across all age groups, there were significant reductions in mean lengths of stay (LOS) between individuals hospitalized for RSV pre-pandemic versus post-pandemic without consideration of ICU admission (pre-pandemic: 6.1 days vs. post-pandemic: 4.7 days; $p = <0.0001$). When stratified by ICU admission, the results differ: while there were no significant reductions between pre-pandemic and post-pandemic mean LOS for anyone requiring ICU admission, there was a general non-significant reduction in mean LOS between pre- versus post-pandemic (7.6 days vs. 6.9 days; $p = 0.3$). [Table 2] Among those not admitted to the ICU, there was a significant reduction in mean LOS after the pandemic compared to before (5.5 days vs. 3.6 days; $p<0.0001$), with the most significant reductions occurring for children under age 2.

*Pandemic impacts on RSV mortality*

Among all time periods, there were 38 deaths out of 3,879 hospitalized RSV patients with outcome data available, having a total hospitalization fatality rate (HFR) of 0.9%. (Table 3). Among those admitted to the ICU (n=1246), there were 22 total deaths resulting in an HFR of 1.8%. The pre-pandemic HFR was 1.5%, while the post-pandemic HFR was 1.9% among all patients with ICU admission. Among patients not admitted to the ICU (n=2633), 16 deaths occurred with a total HFR of 0.6%. The pre-pandemic HFR for non-ICU admitted patients was 0.5%, while the post-pandemic HFR was 0.7%. Patients admitted to the ICU saw a non-significant difference in death post-pandemic compared to pre-pandemic ($\chi2 = 0.3589$, $p = 0.5$). Like the ICU admits, non-ICU admits also saw a non-significant difference in death post-pandemic compared to pre-pandemic ($\chi2 = 0.4$, $p = 0.5$).

**Discussion**

These results show a change in RSV burden from October 2018-December 2022, mostly after the introduction of the COVID-19 pandemic. Before March 2020, RSV was seen as typical and seasonal, later changing after the COVID-19 pandemic began, eventually leading to more cases out of season than cases seen in season in 2021 and 2022. This surge in cases in the summer of 2021 and 2022 coincide with relaxed COVID-19 infection prevention measures and are likely due to a relatively sudden and simultaneous re-exposure of the population to RSV after the COVID-19 pandemic[11–13]. The COVID-19 pandemic's impact on RSV hospitalization burden is positively notable in children, as reflected by their reductions of hospitalization proportions and mean LOS.

Similar to how the COVID-19 pandemic affected RSV incidence, there have been concomitant disruptions to the typical RSV severity profile. While there were no significant changes in mean LOS for hospitalized patients requiring ICU admission, pediatric patients not requiring ICU admission experienced significantly shorter hospital stays after the pandemic than before. The only age groups not to see

significant changes were both adult groups: those aged 18-64 and those over 65. Mortality of RSV saw non-significant changes, with both groups reporting non-significant changes from pre-pandemic to post-pandemic rates, resulting in non-significantly higher rates of death.

Implications of this study include adding to known public health knowledge and epidemiology about RSV, as well as providing insights into changes in trends of RSV severity since the COVID-19 pandemic. RSV remains a leading non-vaccine-preventable cause of illness and death for children under the age of 2 and for older adults, so more completely understanding how a pandemic caused by another respiratory virus impacted both RSV incidence and severity is important for future action[1,6,7,10]. This study provides a baseline for future studies to understand severity changes in their affected populations and can be used by other Emerging Infection Programs nationally, to gain insight into their populations' RSV severity changes due to the COVID-19 pandemic. This study also suggests that institutional and subsequent removal of population-wide disease mitigation measures like mask mandates implemented during the COVID-19 pandemic have substantial indirect effects on RSV burden[11–13]. Intriguingly, considering the high number of hospitalizations for RSV after the pandemic period, the mean reductions in hospital stay length that were observed in this study in the periods following the COVID-19 pandemic are curious and warrant further exploration. This reduction in LOS could be due to increased testing for RSV, resulting in earlier diagnosis, requiring less time in the hospital. Decreased severity may also be explained by detection of more mild or asymptomatic patients that would have not been tested pre-pandemic. Hospitals may have also been overburdened with patients with other illnesses, such as COVID-19, and may have discharged patients sooner than normally needed through a typical RSV admission[12].

Limitations to this study include GAEIP's focus only on hospitalized patients. Since only hospitalized patients were included in this analytic sample, less serious indicators of severity could not be assessed. It is also not possible to determine hospitalization rates from these data, as RSV is not a reportable disease in Georgia. GAEIP surveillance also only conducts surveillance for about 39% of Georgia's population, so results from these analyses could differ if more hospitalizations were included

and/or derived from other states. GAEIP surveillance also covers a mostly urban population, so rural populations are not included in this study. Lastly, since no RSV data was available from April 2020-September 2020 due to the COVID-19 pandemic response, it is possible that RSV-associated hospitalizations were missed. Strengths of the study include a high sample size and uniform completeness of GAEIP hospitalization records. GAEIP also provides data on a diverse group of people, which makes the study informative and generalizable across different demographics.

In conclusion, RSV severity has changed throughout the course of the COVID-19 pandemic and burden of the disease is significantly different now than it was before the pandemic began. Knowledge learned from this study can provide clinicians with better understanding of the prevalence of disease in their area and how trends may be changing due to other pathogen's prevention measures. An RSV vaccine is yet to be approved, as well as an effective antiviral for the disease, which would provide burden reduction for the population.

Tables and Figure

*Table 1. General Demographics of Individuals Hospitalized for Respiratory Syncytial Virus (RSV) infection in Atlanta Metropolitan Area, October 2018 – December 2022*

| *Variable* | Oct 2018 - Mar 2019, n = 720 (%) | Apr 2019 - Sept 2019, n = 29 (%) | Oct 2019 - Mar 2020, n = 930 (%) | Oct 2020 - Mar 2021, n = 19 (%) | Apr 2021 - Sep 2021, n = 749 (%) | Oct 2021 - Mar 2022, n = 352 (%) | Apr 2022 - Sep 2022, n = 778 (%) | Oct 2022 - Dec 2022, n = 436 (28.7) | Total, n = 4013 |
|---|---|---|---|---|---|---|---|---|---|
| *Median Age (years) (IQR)* | 1.6 (26.6) | 1.0 (15) | 2.3 (55.2) | 1.5 (3.9) | 1.4 (2.9) | 4.3 (59.4) | 2.1 (33.7) | 5.0 (61.1) | 2.0 (41.6) |
| *Case Type* | | | | | | | | | |
| *Pediatric Cases* | 535 (74.3) | 22 (75.9) | 605 (65.1) | 16 (84.2) | 646 (86.3) | 209 (59.4) | 568 (73.0) | 245 (56.2) | 2846 |
| *Non-Pediatric Cases* | 185 (25.7) | 7 (24.1) | 325 (34.9) | 3 (15.8) | 103 (13.7) | 143 (40.6) | 210 (27.0) | 191 (43.8) | 116 |
| *Sex* | | | | | | | | | |
| *Male* | 374 (51.9) | 15 (51.7) | 467 (50.2) | 6 (31.6) | 408 (54.5) | 184 (52.3) | 406 (52.2) | 209 (47.9) | 2069 |
| *Female* | 346 (48.1) | 14 (48.3) | 463 (49.8) | 13 (68.4) | 341 (45.5) | 168 (47.7) | 372 (47.8) | 227 (52.1) | 1944 |
| *Race* | | | | | | | | | |
| *White* | 286 (39.7) | 9 (31.0) | 0 | 3 (15.8) | 306 (40.9) | 168 (47.7) | 305 (39.2) | 0 | 1077 |
| *Black or African American* | 342 (47.5) | 17 (58.7) | 0 | 13 (68.4) | 332 (44.3) | 143 (40.6) | 378 (48.6) | 0 | 1225 |
| *Asian/Pacific Islander* | 40 (5.6) | 1 (3.4) | 0 | 0 | 27 (3.6) | 15 (4.3) | 47 (6.0) | 0 | 130 |
| *American Indian/Alaska Native* | 4 (0.6) | 0 | 0 | 0 | 1 (0.1) | 1 (0.3) | 1 (0.1) | 0 | 7 |
| *Multiracial* | 6 (0.8) | 0 | 0 | 0 | 16 (2.1) | 4 (1.1) | 3 (0.4) | 0 | 29 |
| *Unknown* | 42 (5.8) | 2 (6.9) | 930 (100) | 3 (15.8) | 67 (9.0) | 21 (6.0) | 44 (5.7) | 436 (100) | 1545 |
| *Ethnicity* | | | | | | | | | |
| *Hispanic* | 93 (12.9) | 1 (3.5) | 136 (14.6) | 16 (84.2) | 150 (20.0) | 50 (14.2) | 95 (12.2) | 56 (12.8) | 583 |
| *Non-Hispanic* | 615 (85.4) | 27 (93.0) | 784 (84.3) | 2 (10.5) | 594 (79.3) | 301 (85.5) | 676 (86.9) | 375 (86.0) | 3388 |
| *Unknown* | 12 (1.7) | 1 (3.5 | 10 (1.1) | 1 (5.3) | 5 (0.7) | 1 (0.3) | 7 (0.9) | 5 (0.2) | 42 |
| *Pre-existing conditions* | | | | | | | | | |
| *Chronic Lung Disease* | 30 (4.2) | 0 | No Data | 1 (5.3) | 52 (6.9) | 27 (7.7) | 2 (0.3) | No Data | 112 |
| *Chronic Metabolic Disease* | 21 (2.9) | 0 | No Data | 0 | 8 (1.1) | 13 (3.7) | 0 | No Data | 42 |
| *Cardiovascular Disease* | 46 (6.4) | 2 (6.9) | No Data | 2 (10.5) | 34 (4.5) | 19 (5.4) | 0 | No Data | 103 |
| *Blood Disorders* | 6 (0.8) | 0 | No Data | 1 (5.3) | 3 (0.4) | 1 (0.3) | 0 | No Data | 11 |
| *Neurologic Disorders* | 30 (4.2) | 1 (3.4) | No Data | 1 (5.3) | 20 (2.7) | 15 (4.3) | 1 (0.1) | No Data | 68 |
| *Immunocompromised Condition* | 19 (2.6) | 1 (3.4) | No Data | 0 | 3 (0.4) | 3 (0.9) | 0 | No Data | 26 |
| *Renal Disease* | 12 (1.7) | 0 | No Data | 0 | 3 (0.4) | 7 (1.9) | 0 | No Data | 22 |
| *Liver Disease* | 1 (0.1) | 0 | No Data | 0 | 1 (0.1) | 0 | 0 | No Data | 2 |
| *Obesity* | 5 (0.7) | 0 | No Data | 0 | 1 (0.1) | 0 | 0 | No Data | 6 |
| *Premature Birth* | 65 (9.0) | 0 | No Data | 2 (10.5) | 41 (5.5) | 15 (4.3) | 0 | No Data | 123 |

*Figure 1. Proportion of RSV Hospitalizations for RSV Infection by Age Group, October 2018-December 2022*

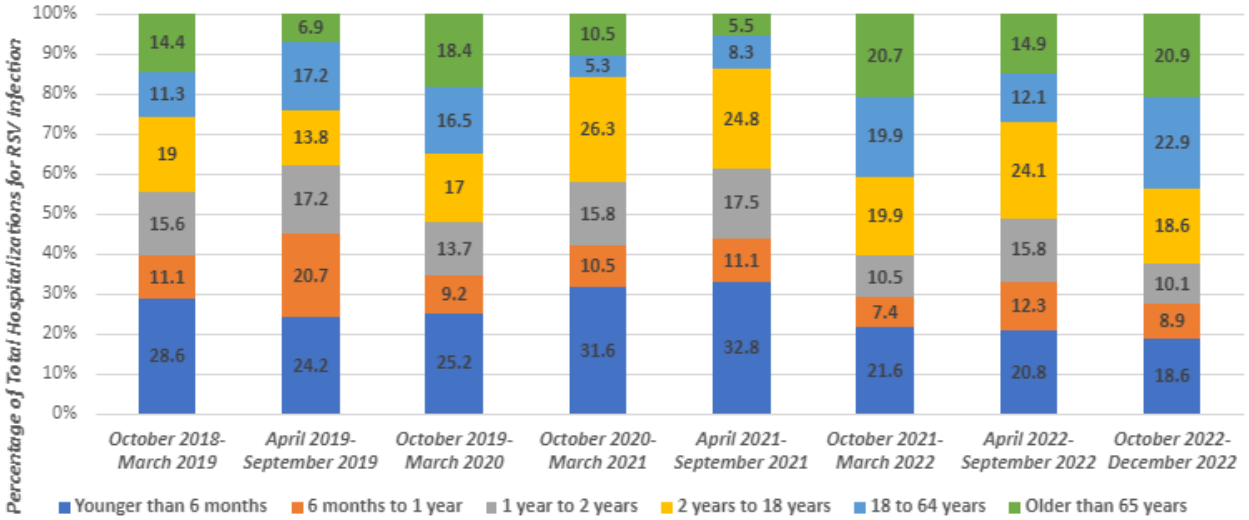

*Table 2. Mean Length (in days) of Hospital Stays for RSV patients by age group, ICU status and COVID-19 pandemic period*

| | ICU admission | | | | No ICU admission | | | |
|---|---|---|---|---|---|---|---|---|
| ***Age Group*** | **Pre-Pandemic n =473 mean (SD)** | **During Pandemic n = 6 mean (SD)** | **Post-Pandemic n = 788 mean (SD)** | **p-value** | **Pre-Pandemic n = 1,206 mean (SD)** | **During Pandemic n = 13 mean (SD)** | **Post-Pandemic n = 1,527 mean (SD)** | **p-value** |
| *Less than 6 months* | 8.3 (10.8) | 8.8 (12.2) | 6.7 (6.8) | 0.05 | 6.2 (16.1) | 3.0 (0) | 2.8 (1.8) | 0.0008 |
| *6 months to 1 year* | 7.3 (13.9) | 0 (0) | 5.7 (6.3) | 0.3 | 4.3 (5.6) | 2.5 (0.7) | 2.9 (2.4) | 0.006 |
| *1 to < 2 years* | 4.4 (2.5) | 22 (0) | 4.7 (3.6) | 0.5 | 3.9 (3.0) | 2.5 (0.7) | 2.7 (2.2) | <0.0001 |
| *2 to 17 years* | 6.3 (7.9) | 18 (0) | 6.1 (7.8) | 0.9 | 5.4 (24.7) | 2.5 (1.3) | 2.6 (1.9) | 0.04 |
| *18 to 64 years* | 17.3 (22.9) | 0 (0) | 14.5 (19.5) | 0.6 | 5.7 (5.7) | 14 (0) | 4.8 (5.6) | 0.06 |
| *Older than 65 years* | 10.2 (7.0) | 0 (0) | 15.3 (16.7) | 0.1 | 5.9 (5.9) | 8.5 (7.8) | 5.5 (4.8) | 0.3 |
| *Total* | 7.6 (10.8) | 12.5 (11.1) | 6.9 (8.8) | 0.3 | 5.4 (13.6) | 4.4 (4.3) | 3.6 (3.7) | <0.0001 |

*Table 3. Mortality among hospitalized RSV patients by ICU admission and pandemic-associated time period*

| | **ICU admission** | | | | **No ICU admission** | | |
|---|---|---|---|---|---|---|---|
| *Outcome* | **Pre-Pandemic** | **Post-Pandemic** | **Total** | | **Pre-Pandemic** | **Post-Pandemic** | **Total** |
| *Dead* | 7 | 15 | 22 | Dead | 6 | 10 | 16 |
| *Alive* | 466 | 758 | 1224 | Alive | 1187 | 1430 | 2617 |
| *Total* | 473 | 773 | 1246 | Total | 1193 | 1440 | 2633 |

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