

1 **TITLE PAGE**

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3 **Full-length title: Decreased mortality associated with respiratory viral infections**

4 **between December 2019 and March 2020 compared to previous year, Southeast France**

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ABSTRACT

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Respiratory viruses are a major global cause of mortality worldwide and in France where they cause several thousands of deaths yearly. University Hospital Institute-Méditerranée Infection performs real-time surveillance of all diagnoses of infections and associated deaths in public hospitals of Marseille, Southeastern France. Here, mortality associated with diagnoses of respiratory viruses was compared during colder months of 2018-2019 and 2019-2020 (week 47-week 11). In 2018-2019, 72 patients (0.16% of 43,909 hospitalized patients) died after being diagnosed with a respiratory virus; 38 and 13 deaths occurred in patients diagnosed with influenza A virus and respiratory syncytial virus (RSV), respectively. In 2019-2020, 44 patients (0.11% of 52,624 patients hospitalized) died after being diagnosed with a common respiratory virus; 6 and 7 deaths occurred in patients diagnosed with influenza A virus and RSV, respectively. Additionally, 11 patients died with a diagnosis of SARS-CoV-2. The proportion of respiratory virus-associated deaths among hospitalized patients was thus significantly lower (-24%) in 2019-2020 than in 2018-2019 ($p= 0.007$). This was majoritarily due to significant decreases of influenza A virus (-84%) and RSV (-46%)-associated deaths, and was not compensated so far by SARS-CoV-2-related deaths. Fatality rate was ≈ 7 times lower in our center than for whole France.

Keywords: Respiratory viruses; mortality; influenza virus; SARS-CoV-2; France

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TEXT

49 Respiratory viruses are a major cause of mortality worldwide with an estimated 2.7 million
50 deaths in 2015 (GBD 2015 LRI Collaborators, 2017). In France, they are causing several
51 thousands of deaths every year during colder months (Pivette et al., 2020). Since January
52 2020, the SARS-CoV-2 outbreak has generated much fear and countermeasures to stem the
53 spread of this respiratory virus. This has been largely fueled by the tremendously extensive
54 reporting of Covid-19-associated deaths. As of March 26, 2020, 492,603 people have been
55 found infected worldwide of whom 22,184 (4.5%) died, four countries (Italy, China, Iran,
56 Spain and France) being concerned by 83% of these deaths
57 (<https://coronavirus.jhu.edu/map.html>). France identified 1,331 deaths for 25,233 infections
58 (5.3%). The University Hospital Institute Méditerranée Infection performs with in-house tools
59 a real-time surveillance of all infections diagnosed in public hospitals of Marseille,
60 Southeastern France (Abat et al., 2015; Roussel et al., 2020). This includes the count of the
61 deaths associated with any diagnosed infection. Here, we compared the mortality associated
62 with diagnoses of respiratory viruses during colder months overlapping 2018-2019 and 2019-
63 2020.

64 Testing of respiratory samples was performed using FTD Respiratory pathogens 21
65 (Fast Track Diagnosis, Luxembourg) or Biofire FilmArray Respiratory panel 2 plus
66 (Biomérieux, France) assays. Between week 47 of 2018 and week 11 of 2019, 72 patients
67 died after being diagnosed with a respiratory virus (Table 1). They represented 0.16% of the
68 43,909 patients hospitalized during this period and 6.9% of the 1,042 who died. Deaths
69 occurred in 38 of the patients diagnosed with influenza A virus (1.7%), which was the
70 respiratory virus associated with the highest number of deaths. In addition, deaths occurred in
71 19 of the patients diagnosed with rhinoviruses (1.8%), and in 13 of those diagnosed with
72 respiratory syncytial virus (RSV) (1.1%). Respiratory samples had not been tested for

73 coronaviruses and parainfluenza viruses in routine clinical practice, but all those tested
74 retrospectively from dead patients were negative. In comparison, during the same period of
75 winter 2019-2020 (between week 47 of 2019 and week 11 of 2020), 44 patients died after
76 being diagnosed with a common respiratory virus. They represented 0.11% of the 52,624
77 patients hospitalized during this period and 5.6% of the 985 who died. They included 6 of the
78 patients diagnosed with influenza A virus (0.4%), 2 of those diagnosed with influenza B virus
79 (0.2%), 7 of those diagnosed with RSV (0.7%), and 4, 2 and 1 of those diagnosed with human
80 coronavirus-HKU1 (1.7%), NL63 (1.2%) and OC43 (1.0%), respectively (Table 1).
81 Additionally, we tested since the 29th of January 13,089 patients for SARS-CoV-2 using a
82 reverse transcription-PCR assay (Amrane et al., 2020), and diagnosed 1,416 infections (11%).
83 Of these infected patients, 11 (0.8%) died until the 25th of March; 8 were ≥ 82 year-old and 5
84 were men.

85 Overall, 55 patients died after being diagnosed with a respiratory virus during colder
86 months of 2019-2020 so far, versus 72 the year before. The proportion of respiratory virus-
87 associated deaths among hospitalized patients was thus significantly lower in 2019-2020 than
88 in 2018-2019 (105 per 100,000 people vs 164 per 100,000 people; $p = 0.007$, Yates-corrected
89 chi-square test). This proportion among patients who died of any cause at hospital was also
90 lower, although not significantly (5.6% vs 6.9%; $p = 0.13$). Hence, we observed 24% less
91 deaths associated with common respiratory viruses during colder months of 2019-2020
92 compared to 2018-2019. This was essentially due to significant decreases of influenza A virus
93 (-84%; $p < 10^{-3}$) and RSV (-46%; $p = 0.055$)-associated deaths among patients diagnosed with
94 these viruses, and was not compensated so far by SARS-CoV-2-related deaths. Excess
95 mortality associated with influenza virus infections is estimated to be 5.9 per 100,000 people
96 worldwide and 5.3 per 100,000 people in Europe (Paget et al., 2019). In comparison, mean
97 mortality associated with SARS-CoV-2 infections is estimated to be 0.3 per 100,000 people

98 worldwide and 2.2 per 100,000 people in Western Europe (<https://www.mediterranee->
99 [infection.com/covid-19/](https://www.mediterranee-infection.com/covid-19/)). These data and our findings allow putting into perspective the
100 current death burden of SARS-CoV-2 infections. Finally, we observed that fatality rate was
101 ≈ 7 times lower in our center than for whole France that has a very high fatality rate of 2.6 per
102 100,000 people.

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105 **Author contributions**

106 Conceived and designed the review: DR. Contributed materials/analysis tools: AG, PC, MTJ,
107 CZ, LN, CB, JCL, BLS, HC. Analyzed the data: AG, PC, DR. Wrote the paper: AG, PC, DR.

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116 **Conflicts of interest**

117 The authors have no conflicts of interest to declare. Funding sources had no role in the design
118 and conduct of the study; collection, management, analysis, and interpretation of the data; and
119 preparation, review, or approval of the manuscript.

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121 **Ethical approval**

122 Not required. All data have been generated as part of the routine work at Assistance Publique-

123 Hôpitaux de Marseille (Marseille university hospitals), and this study results from routine
124 standard clinical management.

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TABLE**Table 1.** Tests performed and positive for PCR detection of respiratory viruses, and associated deaths during same colder months overlapping years 2018-2019 and 2019-2020

Viruses	Tests		Positive patients				Deaths				P ^a
	2018-2019	2019-2020	2018-2019		2019-2020		2018-2019		2019-2020		
	Number	Number	Number	%	Number	%	Number	%	Number	%	
Adenovirus	11 004	13 462	439	4.0	426	3.2	2	0.5	4	0.9	
Coronavirus HKU1	-	7 461	-	-	236	3.2	-	-	4	1.7	
Coronavirus NL63	-	7 461	-	-	162	2.2	-	-	2	1.2	
Coronavirus OC43	-	7 461	-	-	102	1.4	-	-	1	1.0	
Coronavirus E229	-	7 461	-	-	57	0.8	-	-	0	0.0	
SARS-CoV-2 ^b	-	13 089	-	-	1 416	10.8	-	-	11	0.8	
Enterovirus	11 004	13 462	308	2.8	356	2.6	0	0.0	2	0.6	
Influenza A virus	11 004	13 462	2 277	20.7	1 516	11.3	38	1.7	6	0.4	<10 ⁻³
Influenza B virus	11 004	13 462	13	0.1	1 220	9.1	0	0.0	2	0.2	
Metapneumovirus	11 004	13 462	306	2.8	449	3.3	0	0.0	2	0.4	
Parainfluenza virus 1	-	7 461	-	-	6	0.1	-	-	0	0.0	
Parainfluenza virus 2	-	7 461	-	-	6	0.1	-	-	0	0.0	
Parainfluenza virus 3	-	7 461	-	-	8	0.1	-	-	0	0.0	
Parainfluenza virus 4	-	7 461	-	-	22	0.3	-	-	0	0.0	
Rhinovirus	11 004	13 462	1 073	9.8	1 459	10.8	19	1.8	14	1.0	0.055
Syncytial respiratory virus	11 004	13 462	1 135	10.3	1 040	7.7	13	1.1	7	0.7	0.177

^a Assessed for proportions of deaths among positive patients; Yates-corrected chi-square test; ^b until 25th of March, 2020