



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Short Communication

Comparison of mortality associated with respiratory viral infections between December 2019 and March 2020 with that of the previous year in Southeastern France



Audrey Giraud-Gatineau^{a,b,c,1}, Philippe Colson^{a,d,1}, Marie-Thérèse Jimeno^e, Christine Zandotti^{a,f}, Laetitia Ninove^{a,f}, Céline Boschi^{a,d}, Jean-Christophe Lagier^{a,d}, Bernard La Scola^{a,d}, Hervé Chaudet^{a,b,c}, Didier Raoult^{a,d,*}

^a IHU Méditerranée Infection, Marseille, France

^b Aix Marseille Univ, Institut de Recherche pour le Développement (IRD), Assistance Publique - Hôpitaux de Marseille (AP-HM), Service de Santé des Armées (SSA), Vecteurs - Infections Tropicales et Méditerranéennes (VITROME), Marseille, France

^c French Armed Forces Center for Epidemiology and Public Health (CESPA), Service de Santé des Armées (SSA), Marseille, France

^d Aix-Marseille Univ., Institut de Recherche pour le Développement (IRD), Assistance Publique - Hôpitaux de Marseille (AP-HM), Microbes Evolution Phylogeny and Infections (MEPHI), Marseille, France

^e Service de l'Information Médicale, Hôpital de la Timone, Marseille, France

^f Unité des Virus Emergents (UVE), Aix-Marseille University, IRD 190, Inserm 1207, IHU Méditerranée Infection, Marseille, France

ARTICLE INFO

Article history:

Received 29 March 2020

Received in revised form 25 April 2020

Accepted 1 May 2020

Keywords:

Respiratory viruses

Mortality

Influenza virus

SARS-CoV-2

France

ABSTRACT

Respiratory viruses are a major cause of mortality worldwide and in France, where they cause several thousands of deaths every year. University Hospital Institute-Méditerranée Infection performs real-time surveillance of all diagnoses of infections and associated deaths in public hospitals in Marseille, Southeastern France. This study compared mortality associated with diagnoses of respiratory viruses during the colder months of 2018–2019 and 2019–2020 (week 47–week 14). In 2018–2019, 73 patients (0.17% of 42,851 hospitalized patients) died after being diagnosed with a respiratory virus; 40 and 13 deaths occurred in patients diagnosed with influenza A virus and respiratory syncytial virus (RSV), respectively. In 2019–2020, 50 patients (0.10% of 49,043 patients hospitalized) died after being diagnosed with a common respiratory virus; seven and seven deaths occurred in patients diagnosed with influenza A virus and RSV, respectively. Additionally, 55 patients died after being diagnosed with SARS-CoV-2. The proportion of respiratory virus-associated deaths among hospitalized patients was thus significantly lower for common respiratory viruses in 2019–2020 than in 2018–2019 (102 versus 170 per 100,000 hospitalized patients; $p = 0.003$), primarily as a consequence of a decrease in influenza A virus (–83%) and RSV (–46%) associated deaths. Overall, the proportion of respiratory virus-associated deaths among hospitalized patients was higher, but not significantly, in 2019–2020 than in 2018–2019 (214 versus 170 per 100,000 hospitalized patients; $p = 0.08$, Yates-corrected Chi-square test). These findings put into perspective the death burden of SARS-CoV-2 infections in this geographical area.

© 2020 Published by Elsevier Ltd on behalf of International Society for Infectious Diseases. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Respiratory viruses are a major cause of mortality worldwide, with an estimated 2.7 million deaths in 2015 (GBD 2015 LRI Collaborators, 2017). In France, they cause several thousands of deaths every year during the colder months (Pivette et al., 2020). Since January 2020, the SARS-CoV-2 outbreak has generated much fear and countermeasures to stem the spread of this respiratory

virus. This has largely been fueled by the tremendously extensive reporting of Covid-19-associated deaths. As of 31 March 2020, 770,520 people have been found infected worldwide, of whom 36,942 (4.8%) died. Five countries (Italy, Spain, China, USA and France) have been affected by 77% of these deaths (<https://coronavirus.jhu.edu/map.html>). France identified 3,024 deaths for 44,450 infections (6.8%). The University Hospital Institute Méditerranée Infection performs, with in-house tools, a real-time surveillance of all infections in public hospitals in Marseille, Southeastern France (Abat et al., 2015; Roussel et al., 2020). This surveillance allows weekly analysis of the numbers of each type of clinical sample received and any pathogen diagnosed at the

* Corresponding author at: IHU Méditerranée Infection, 19-21 boulevard Jean Moulin, 13005 Marseille, France.

E-mail address: didier.raoult@gmail.com (D. Raoult).

¹ Contributed equally.

laboratory, including respiratory samples and viruses, and performing retrospective analyses that include the most recently available data. It also includes the count of the deaths associated with any diagnosed infection. This study compared the mortality associated with diagnoses of respiratory viruses during the colder months overlapping 2018–2019 and 2019–2020.

Testing of respiratory samples was performed using FTD Respiratory pathogens 21 (Fast Track Diagnosis, Luxembourg) or Biofire FilmArray Respiratory panel 2 plus (Biomérieux, France) assays. Between week 47 of 2018 and week 14 of 2019, 73 patients died after being diagnosed with respiratory viruses (Table 1). They represented 0.17% of the 42,851 patients hospitalized during this period and 6.3% of the 1,137 who died. Deaths occurred in 40 of the patients diagnosed with influenza A virus (1.7%), which was the respiratory virus associated with the highest number of deaths. In addition, deaths occurred in 19 of the patients diagnosed with rhinoviruses (1.5%), and in 13 of those diagnosed with respiratory syncytial virus (RSV) (1.1%). Respiratory samples had not been tested for coronaviruses and parainfluenza viruses in routine clinical practice, but all those retrospectively tested from patients who died in Marseille public hospitals were negative. In comparison, during the same period of winter 2019–2020 (between week 47 of 2019 and week 14 of 2020), 50 patients died after being diagnosed with a common respiratory virus. They represented 0.10% of the 49,043 patients hospitalized during this period and 4.5% of the 1,115 who died. They included seven of the patients diagnosed with influenza A virus (0.5%), three of those diagnosed with influenza B virus (0.2%), seven of those diagnosed with RSV (0.7%), and six, two and one of those diagnosed with human coronavirus-HKU1 (2.4%), NL63 (1.2%) and OC43 (0.8%), respectively (Table 1). Additionally, since the 29 January 2020, 25,786 patients were tested for SARS-CoV-2 using a reverse transcription-PCR assay (Amrane et al., 2020), and 3,587 infections were diagnosed positive (13.9%). Of these infected patients, 55 (1.5%) died; their median age was 82 years.

Thus, a total of 105 patients died after being diagnosed with a respiratory virus during the colder months of 2019–2020 until week 14 of 2020 compared with 73 the year before during the same timeframe (+44%). However, the proportion of respiratory virus-associated deaths among hospitalized patients did not significantly differ in 2019–2020 and 2018–2019 (214 versus 170 per 100,000 hospitalized patients; $p = 0.08$, Yates-corrected Chi-square test). In contrast, it was significantly lower in 2019–2020 than in

2018–2019 for common respiratory viruses (102 versus 170 per 100,000 hospitalized patients; $p = 0.003$), which were associated with 33% fewer deaths in 2019–2020. This drop was essentially due to a significant decrease in influenza A virus-associated deaths (–84%; $p < 0.001$) and a decrease in RSV-associated deaths (–46%; $p = 0.18$) among patients diagnosed with these viruses. The drop in influenza-associated deaths could be partly explained by the predominance of A/H3N2 strains in 2018–2019 compared with the predominance of A/H1N1 and B strains in 2019–2020, as A/H3N2 strains were reported to be associated with a greater mortality in elderly people (Lemaitre et al., 2012; Paget et al., 2019). A 21% drop in the number of deaths in patients diagnosed with rhinovirus, and a reduction from 1.5% to 1% of the proportion of deaths among diagnosed patients ($p = 0.11$) was also observed in 2019–2020 compared with 2018–2019.

Overall, these findings put into perspective the death burden of SARS-CoV-2 infections in this geographical area. Thus, the number of SARS-CoV-2-associated deaths was similar to that of deaths associated with other viral respiratory infections between December 2019 and March 2020, and lower than that of deaths associated with viral respiratory infections between December 2018 and March 2019. In addition, no significant impact of SARS-CoV-2 infections was observed on the overall number of deaths (of any cause) among hospitalized people in Marseille public hospitals (1,115 deaths in 2019–2020 during the study period versus 1,137 in 2018–2019; Figure 1a), or in the population of metropolitan France (175,384 deaths in 2019–2020 versus 173,923 in 2018–2019; Figure 1b; <https://www.insee.fr/fr/statistiques/serie/000436394#Telechargement>). Further analyses might determine if this is related to containment or other changes related to the SARS-CoV-2 epidemics. The number of SARS-CoV-2-associated deaths will grow after the timeframe of the present study as a consequence of recent or new infections, but the peak of incidence of SARS-CoV-2 infections was reached at the end of March 2020 in Marseille public hospitals (<https://www.mediterranee-infection.com/covid-19/>) and in metropolitan France (<https://www.santepubliquefrance.fr/content/download/246357/2578114>).

Author contributions

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

Table 1

Tests performed and positive for PCR detection of respiratory viruses, and associated deaths during the same colder months overlapping the years 2018–2019 and 2019–2020.

Viruses	Tests		Positive patients				Deaths				<i>P</i> ^a
	2018–2019	2019–2020	2018–2019		2019–2020		2018–2019		2019–2020		
	Number	Number	Number	%	Number	%	Number	%	Number	%	
Adenovirus	11,922	16,098	475	4.0	448	2.8	2	0.4	4	0.9	<0.001
Coronavirus HKU1	–	10,097	–	–	253	2.5	–	–	6	2.4	
Coronavirus NL63	–	10,097	–	–	173	1.7	–	–	2	1.2	
Coronavirus OC43	–	10,097	–	–	120	1.2	–	–	1	0.8	
Coronavirus E229	–	10,097	–	–	69	0.7	–	–	0	0.0	
SARS-CoV-2	–	42,242	–	–	3,587	8.5	–	–	55	1.5	
Enterovirus	11,922	16,098	343	2.9	362	2.3	1	0.3	2	0.6	
Influenza A virus	11,922	16,098	2,293	19.2	1,554	9.7	40	1.7	7	0.5	
Influenza B virus	11,922	16,098	15	0.1	1,261	7.8	0	0.0	3	0.2	
Metapneumovirus	11,922	16,098	346	2.9	472	2.9	0	0.0	5	1.1	
Parainfluenza virus 1	–	10,097	–	–	7	0.1	–	–	0	0.0	0.11
Parainfluenza virus 2	–	10,097	–	–	12	0.1	–	–	0	0.0	
Parainfluenza virus 3	–	10,097	–	–	11	0.1	–	–	0	0.0	
Parainfluenza virus 4	–	10,097	–	–	30	0.3	–	–	0	0.0	
Rhinovirus	11,922	16,098	1,241	10.4	1,565	9.7	19	1.5	15	1.0	
Syncytial respiratory virus	11,922	16,098	1,146	9.6	1,044	6.5	13	1.1	7	0.7	

^a Assessed for proportions of deaths among positive patients; Yates-corrected Chi-square test.

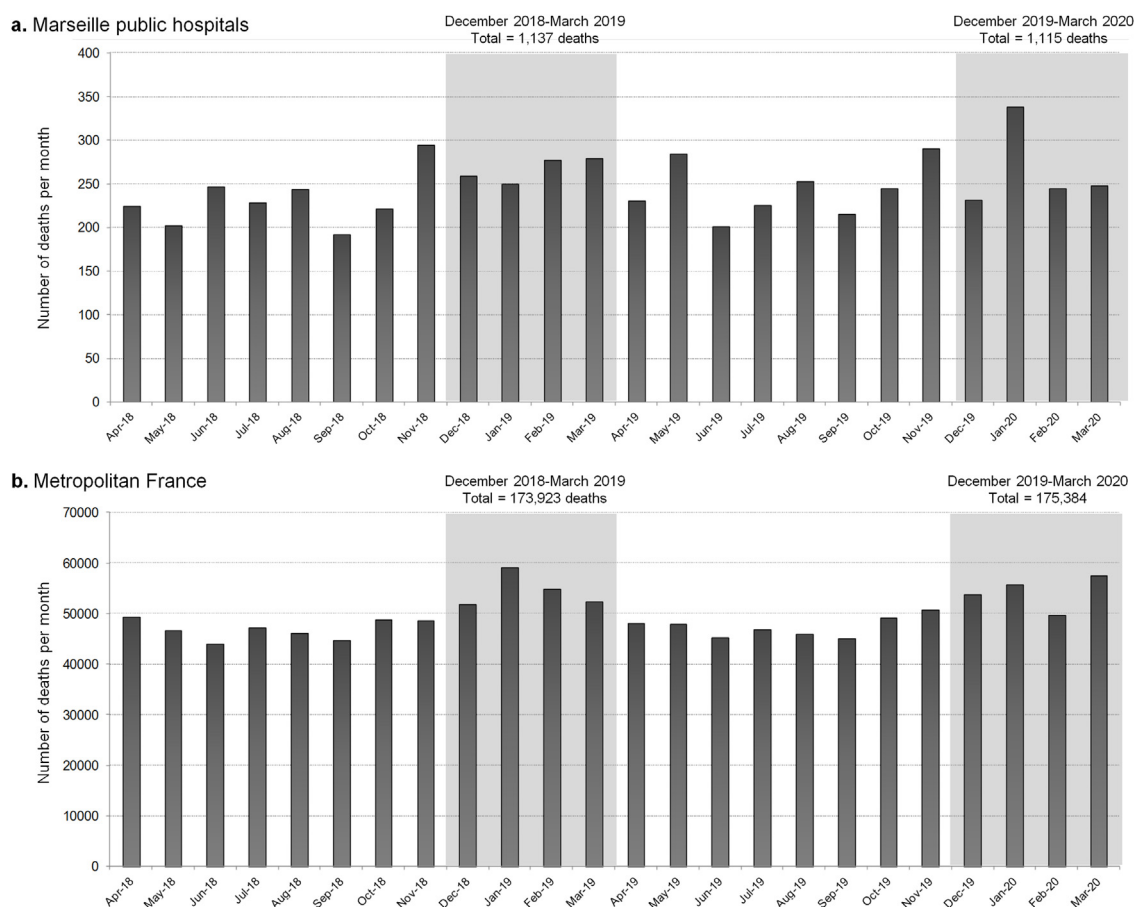


Figure 1. Number of deaths of any cause per month in Marseille public hospitals (a) and in Metropolitan France (<https://www.insee.fr/fr/statistiques/serie/000436394#Telechargement>) (b). Periods of time analysed in the present study are indicated by the rectangles with a grey background.

Funding

This work was supported by the French Government under the “Investments for the Future” program managed by the National Agency for Research (ANR) (No. Méditerranée-Infection10-IAHU-03) and was also supported by Région Provence-Alpes-Côte d’Azur and European funding FEDER PRIMMI (Fonds Européen de Développement Régional - Plateformes de Recherche et d’Innovation Mutualisées Méditerranée Infection).

Conflicts of interest

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

Ethical approval

Not required. All data have been generated as part of the routine work at Assistance Publique-Hôpitaux de Marseille (Marseille university hospitals), and this study results from routine standard clinical management.

Acknowledgments

We are grateful to the reviewers for the valuable comments that improved this manuscript.

References

- Abat C, Chaudet H, Colson P, Rolain JM, Raoult D. Real-time microbiology laboratory surveillance system to detect abnormal events and emerging infections, Marseille, France. *Emerg Infect Dis* 2015;21:1302–10.
- Amrane S, Tissot-Dupont H, Doudier B, Eldin C, Hocquart M, Mailhe M, et al. Rapid viral diagnosis and ambulatory management of suspected COVID-19 cases presenting at the infectious diseases referral hospital in Marseille, France, - January 31st to March 1st, 2020: a respiratory virus snapshot. *Travel Med Infect Dis* 2020;101632.
- GBD 2015 LRI Collaborators. Estimates of the global, regional, and national morbidity, mortality, and aetiologies of lower respiratory tract infections in 195 countries: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet Infect Dis* 2017;17:1133–61.
- Lemaitre M, Carrat F, Rey G, Miller M, Simonsen L, Viboud C. Mortality burden of the 2009 A/H1N1 influenza pandemic in France: comparison to seasonal influenza and the A/H3N2 pandemic. *PLoS One* 2012;7:e45051.
- Paget J, Spreuwenberg P, Charu V, Taylor RJ, Iuliano AD, Bresee J, et al. Global mortality associated with seasonal influenza epidemics: new burden estimates and predictors from the GLAMOR Project. *J Glob Health* 2019;9:020421.
- Pivette M, Nicolay N de L V, Hubert B. Characteristics of hospitalizations with an influenza diagnosis, France, 2012–2013 to 2016–2017 influenza seasons. *Influenza Other Respir Viruses* 2020;(February). doi:<http://dx.doi.org/10.1111/irv.12719> [Epub ahead of print].
- Roussel Y, Giraud-Gatineau A, Jimeno MT, Rolain JM, Zandotti C, Colson P, et al. SARS-CoV-2: fear versus data. *Int J Antimicrob Agents* 2020;105947.