JIM Research Letter

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Progressive decrease of the healthcare impact of the post-COVID condition after the first disease wave in Lombardy, Italy

Dear Editor,

The northern Italian region of Lombardy (population 10 million) was the first large European area to be heavily hit in the early months of 2020 by the first wave of the SARS-CoV-2 pandemic due to the original Wuhan coronavirus strain. During the period of March to May, the total number of deaths registered in Lombardy increased by 111% [1] in comparison with the average number in the same months of 2015–2019. This gloomy scenario led us to consider the region as a model to evaluate the impact of the sequels of the pandemic (the so-called "post-COVID condition") [2] on the healthcare service of the region by using the administrative claims database made available to us for academic purposes. In a previous report [3] based on 48,148 patients who survived the infection and became SARS-CoV-2 polymerase chain reaction (PCR) negative by 30 June 2020, 768 of them (1.6%) died in the early post-COVID semester of July to December 2020, 4171 (8.6%) were admitted to hospital medical wards for reasons other than reinfection with SARS-CoV-2, 10,357 (21.5%) attended a hospital emergency room without subsequent admission, and 33,570 (70%) made use of outpatient medical visits [2]. We have also demonstrated as a comparison point that nonfatal events leading to the use of the regional health service—hospitalizations and emergency room and outpatient medical visits—were much more frequent than in the corresponding semester of 2019, when the region was not yet hit by the pandemic [3].

We have here accrued the claims data corresponding to a much longer time period after SARS-CoV-2 PCR negativization—that is, in the two semesters from January to December 2021. Thus, we chose to compare the number of deaths and reasons for use of the facilities of the regional health service with those recorded in the first post-negativization semester but also in the corresponding semester of the 2019 prepandemic period as a suitable comparison point. Our goal was to gain insights into whether the impact of the post-COVID condition was confined to the first 6 months after SARS-CoV-2 PCR negativization or whether it continued to burden the regional health service for a longer time period and more frequently and heavily than before the pandemic [3].

Table 1 shows for two 2021 semesters the number and rates of incident deaths, hospitalizations, emergency room attendances, and outpatient medical visits for the whole cohort of 48,148 patients who survived SARS-CoV-2 infection and became PCR-test negative. Also shown are subgroups split according to the site of management of the acute infection—home, nonintensive care medical wards, and intensive care units with mechanical ventilation. Data are also presented as adjusted hazard ratios with reference to the pre-COVID comparison period of 2019. For all cases—but also for cases split according to the site of management—deaths were roughly halved in comparison with the July to December 2020 semester. Moreover, hospitalizations, emergency room attendance, and outpatient medical visits were much less prevalent than in the early post-COVID semester and were similar to those recorded in the regional database in the corresponding months of the 2019 pre-COVID period.

Overall, these data show that—at least in a region such as Lombardy affected by dramatic and unprecedented mayhem—the post-COVID condition became much less prominent after the first 6 months had elapsed since SARS-CoV-2 PCR negativization. The claims data presented here are based on objective events with healthcare impact such as deaths, hospitalizations, and need for emergency room and outpatient medical visits, but fail to provide direct information on the post-COVID burden of subjective symptoms such as fatigue, anxiety, and depression and on patient proficiency in the activities of daily living and

Table 1. *Comparison of post-COVID impact on the major condition during three semesters up to 31 December 2021, after SARS-CoV-2 polymerase-chain-reaction negativization, in all survivors, those treated at home, those hospitalized, and those admitted to the intensive care unit (ICU)*

Variables	At home *N* = 20,521	Hospitalized *N* = 26,016	ICU *N* = 1611	All survivors *N* = 48,148
Died	*N* (%)	*N* (%)	*N* (%)	*N* (%)
On 31 December 2020, 6 months after swab negativization	236 (1.2)	520 (2.0)	12 (0.7)	768 (1.6)
From 1 January 2021 to 30 June 2021	138 (0.7)	267 (1.1)	6 (0.4)	411 (0.9)
From 1 July 2021 to 31 December 2021	123 (0.6)	267 (1.1)	5 (0.3)	395 (0.8)
Cases rehospitalized	*N* (%)	*N* (%)	*N* (%)	*N* (%)
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% C.I.)
July to December 2019	1057 (5.2)	2204 (8.5)	64 (4.0)	3325 (6.9)
	1	1	1	1
On 31 December 2020, 6 months after swab negativization	1079 (5.3)	2830 (10.9)	262 (16.3)	4171 (8.7)
	1.03 (0.93–1.13)	1.39 (1.31–1.49)	6.01 (4.41–8.18)	1.34 (1.27–1.41)
From 1 January 2021 to 30 June 2021	915 (4.5)	1995 (7.8)	111 (6.9)	3021 (6.4)
	0.87 (0.79–0.96)	0.93 (0.87–0.99)	1.95 (1.39–2.72)	0.93 (0.88–0.98)
From 1 July 2021 to 31 December 2021	996 (4.9)	2073 (8.2)	122 (7.7)	3191 (6.8)
	0.98 (0.89–1.08)	1.004 (0.94–1.08)	2.22 (1.59–3.08)	1.02 (0.96–1.08)
Cases attending a hospital emergency room without subsequent hospitalization	*N* (%)	*N* (%)	*N* (%)	*N* (%)
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
July to December 2019	2442 (11.9)	3934 (15.1)	175 (10.9)	6551 (13.6)
	1	1	1	1
On 31 December 2020, 6 months after swab negativization	2832 (13.8)	5066 (19.5)	259 (16.1)	8157 (16.9)
	1.21 (1.14–1.29)	1.42 (1.35–1.49)	1.68 (1.34–2.09)	1.35 (1.30–1.40)
From 1 January 2021 to 30 June 2021	2153 (10.6)	3208 (12.6)	184 (11.5)	5545 (11.7)
	0.87 (0.81–0.93)	0.79 (0.75–0.83)	1.08 (0.85–1.36)	0.83 (0.79–0.86)
From 1 July 2021 to 31 December 2021	2375 (11.8)	3545 (14.1)	156 (9.8)	6076 (12.9)
	0.99 (0.93–1.06)	0.91 (0.87–0.96)	0.88 (0.69–1.12)	0.94 (0.90–0.98)
Cases of patients who underwent a specialist visit	*N* (%)	*N* (%)	*N* (%)	*N* (%)
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
July to December 2019	7592 (37.0)	13,209 (50.8)	647 (40.2)	21,448 (44.6)
	1	1	1	1
On 31 December 2020, 6 months after swab negativization	8343 (40.7)	17,524 (67.4)	1352 (83.9)	27,219 (56.5)
	1.25 (1.19–1.31)	2.69 (2.56–2.81)	15.63 (12.65–19.31)	2.03 (1.97–2.09)

(*Continued*)

Table 1. *(Continued)*

Variables	At home *N* = 20,521	Hospitalized *N* = 26,016	ICU *N* = 1611	All survivors *N* = 48,148
From 1 January 2021 to 30 June 2021	7342 (36.2)	13,576 (53.3)	1024 (64.0)	21,942 (46.3)
	0.96 (0.91–1.002)	1.16 (1.11–1.20)	3.80 (3.19–4.52)	1.11 (1.08–1.15)
From 1 July 2021 to 31 December 2021	7340 (36.4)	12,771 (50.6)	850 (53.4)	20,961 (44.6)
	0.97 (0.93–1.02)	0.997 (0.96–1.04)	2.08 (1.76–2.45)	1.01 (0.98–1.04)
Number of drugs	Mean (SD) Median (IQR) Difference (95% CI)	Mean (SD) Median (IQR) Difference (95% CI)	Mean (SD) Median (IQR) Difference (95% CI)	Mean (SD) Median (IQR) Difference (95% CI)
July to December 2019	1.6 (2.6)	3.4 (3.7)	2.5 (2.9)	2.6 (3.4)
	1 (0–2)	2 (0–5)	2 (0–4)	1 (0–4)
On 31 December 2020, 6 months after swab negativization	1.9 (2.9)	4.3 (4.2)	5.1 (4.0)	3.3 (3.9)
	1 (0–3)	3 (1–7)	4 (2–7)	2 (0–5)
	+0.23 (0.20–0.25)	+0.90 (0.87–0.93)	+2.59 (2.46–2.71)	+0.67 (0.65–0.69)
From 1 January 2021 to 30 June 2021	1.7 (2.7)	3.7 (3.8)	3.6 (3.5)	2.8 (3.5)
	1 (0–2)	3 (0–6)	3 (1–5)	1 (0–4)
	+0.06 (0.03–0.08)	+0.37 (0.34–0.40)	+1.09 (0.96–1.21)	+0.26 (0.24–0.28)
From 1 July 2021 to 31 December 2021	1.7 (2.7)	3.7 (3.8)	3.6 (3.6)	2.8 (3.5)
	1 (0–2)	3 (0–6)	3 (1–6)	2 (0–4)
	+0.10 (0.08–0.13)	+0.41 (0.38–0.44)	+1.12 (0.99–1.25)	+0.30 (0.28–0.32)
Polypharmacy	*N* (%) OR (95% CI)	*N* (%) OR (95% CI)	*N* (%) OR (95% CI)	*N* (%) OR (95% CI)
July to December 2019	2407 (11.7)	8029 (30.9)	335 (20.8)	10,771 (22.4)
	1	1	1	1
On 31 December 2020, 6 months after swab negativization	2821 (13.8)	10,230 (39.3)	794 (49.3)	13,845 (28.8)
	1.79 (1.61–1.99)	3.28 (3.07–3.51)	26.23 (19.40–35.48)	3.06 (2.89–3.23)
From 1 January 2021 to 30 June 2021	2429 (12.0)	8822 (34.6)	522 (32.7)	11,773 (24.9)
	1.19 (1.07–1.32)	1.83 (1.71–1.95)	4.46 (3.43–5.79)	1.71 (1.62–1.81)
From 1 July 2021 to 31 December 2021	2425 (12.0)	8639 (34.2)	525 (33.0)	11,589 (24.7)
	1.31 (1.17–1.46)	1.83 (1.71–1.96)	4.61 (3.55–6.00)	1.76 (1.66–1.86)

Note: Logistic and linear random-intercept model in each cohort.
Abbreviations: CI, confidence interval; IQR, interquartile range; OR, odds ratio; SD, standard deviation.

quality of life. A recent report from Wuhan in China on the follow-up for up to 2 years of 1192 patients who survived hospitalization after the first COVID-19 wave showed that the burden of subjective symptoms continued to be substantially higher than in Wuhan residents without COVID-19 matched with cases for sex, age, and comorbidities [4]. Because both the Wuhan and the present cohort refer to the first wave of exposure as an unprecedented and unexpected infection, it remains to be established whether the early burden of the post-COVID condition is going to be

different following the subsequent waves of COVID-19, when more knowledge was accrued on disease management and vaccines became available at least in high-income countries.

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Conflict of interest

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Author contributions

Pier M. Mannucci: Conceptualization; Methodology; Writing – original draft. Alessandro Nobili: Conceptualization; Methodology; Writing – original draft; Writing – review and editing. Mauro Tettamanti: Conceptualization; Data curation; Formal analysis; Methodology; Writing – review and editing. Barbara D'Avanzo: Methodology; Writing – original draft; Writing – review and editing. Alessia A. Galbussera: Data curation; Formal analysis; Writing – review and editing. Giuseppe Remuzzi: Supervision; Writing – review and editing. Ida Fortino: Supervision; Writing – review and editing. Olivia Leoni: Supervision; Writing – review and editing. Sergio Harari: Conceptualization; Writing – original draft; Writing – review and editing.

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References

1 ISTAT. Impatto dell'epidemia covid-19 sulla mortalità totale della popolazione residente. https://www.istat.it/it/files/2021/03/Report_ISS_Istat_2020_5_marzo.pdf (2020). Accessed 13 April 2022.

2 CDC NCHS. CDC announces approval of ICD-10 code for post-acute sequelae of COVID-19. https://www.cdc.gov/nchs/icd/icd10cm.htm (2022). Accessed 13 Apr 2022.

3 Mannucci PM, Nobili A, Tettamanti M, D'Avanzo B, Galbussera AA, Remuzzi G, et al. Impact of the post-COVID-19 condition on health care after the first disease wave in Lombardy. *J Intern Med.*. 2022;**292**:450–62. doi: 10.1111/joim.13493

4 Huang L, Li X, Gu X, Zhang H, Ren L, Guo L, et al. Health outcomes in people 2 years after surviving hospitalisation with COVID-19: a longitudinal cohort study. *Lancet Respir Med.*. 2022. doi: 10.1016/S2213-2600(22)00126-6

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