

# BMJ Open Mortality and healthcare assessment among patients with chronic disease over 2 years of COVID-19: a population-based study in a large hard-hit Italian region

Daniela Fortuna <sup>1</sup>, Luana Caselli,<sup>1</sup> Elena Berti,<sup>1</sup> Maria Luisa Moro<sup>2</sup>

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<sup>1</sup>Innovation in Healthcare and Social Services, Emilia-Romagna Region, Bologna, Emilia-Romagna, Italy

<sup>2</sup>Regional Agency for Health and Social Care, Emilia-Romagna Region, Bologna, Emilia-Romagna, Italy

## Correspondence to

Dr Daniela Fortuna;  
daniela.fortuna@regione.emilia-romagna.it

## ABSTRACT

**Objectives** We aimed to provide a region-wide comprehensive account of the indirect effects of COVID-19 on patients with chronic disease, in terms of non-COVID-19 mortality, and access to both inpatient and outpatient health services over a 2-year pandemic period.

**Design** Population-based retrospective study.

**Setting** Adult patients, affected by at least 1 of 32 prevalent chronic conditions, residing in the Emilia-Romagna Region in Italy, during the years 2020 (N=1 791 189, 47.7% of the overall adult regional population) and 2021 (N=1 801 071, 47.8%).

**Results** Overall, non-COVID-19 mortality among patients with chronic disease during the pandemic (2.7%) did not differ substantially from the expected mortality (2.5%), based on a 3 years prepandemic period (2017–2019) and adjusting for the demographic and clinical characteristics of the population under study. Indeed, while the first pandemic wave was characterised by a significant non-COVID-19 excess mortality (March: +35%), the subsequent phases did not show such disruptive variations in non-COVID-19 deaths, which remained around or even below the excess mortality threshold. End-of-life care of patients with chronic disease, especially for non-COVID-19 cases, significantly shifted from hospitalisations (–19%), to homecare (ADI: +7%; w/o ADI: +9%). Overall, healthcare of patients without COVID-19 chronic disease decreased, with similar negative trends in hospitalisations (–15.5%), major procedures (–19.6%) and ER accesses (–23.7%). Homecare was the least affected by the pandemic, with an overall reduction of –9.8%. COVID-19 outbreak also impacted on different types of outpatient care. Rehabilitation therapies, specialist visits, diagnostic and lab tests were considerably reduced during the first pandemic wave and consequent lockdown, with access rates of patients without COVID-19 chronic disease below –60%.

**Conclusions** This work thoroughly describes how a large and well-defined population of patients without COVID-19 chronic disease has been affected by the changes and reorganisation in the healthcare system during 2 years of the pandemic, highlighting health priorities and challenges in chronic disease management under conditions of limited resources.

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This study used data derived from 15 different regional databases to provide an up-to-date and comprehensive overview of the indirect effects of COVID-19 on patients with non-infected chronic disease.
- ⇒ This is a large population-based study, representative of all patients with chronic disease residing in a vast region of Italy, among the most affected by the pandemic.
- ⇒ We estimated observed/expected time trends in non-COVID-19 mortality and healthcare use among patients with chronic disease over 2020 and 2021, based on a reference 3-year prepandemic period.
- ⇒ As this is a retrospective study based on administrative data, possible errors in the reporting of COVID-19-related diagnoses or deaths might have influenced the non-COVID-19 outcome estimates reported here.
- ⇒ This study was conducted at the regional level, and this aspect should be considered before extrapolating and generalising results to other populations.

## BACKGROUND

The impact of the COVID-19 pandemic on patients with underlying chronic conditions has been particularly significant in terms of disease severity and mortality.<sup>1–3</sup> It is now widely established that age, type and number of comorbidities are important predictors for adverse outcomes from SARS-CoV-2 infection.<sup>4</sup> Recently, several studies have suggested the need for a more comprehensive picture of the pandemic crisis, as the impact of COVID-19 on global health is underestimated if only the effects directly attributed to the disease are considered.<sup>5 6</sup> All-cause excess mortality was registered across countries during the pandemic, indicating that a relevant proportion of deaths was likely the result of exacerbated non-COVID-19 medical



conditions, that remained undiagnosed or untreated.<sup>7</sup> These are known as indirect effects of the pandemic and include a range of health outcomes subsequent to lack of preventative care, delays in diagnosis of new diseases and disruptions to treatment, which were shown to have particularly serious implications for people with pre-existing medical conditions.<sup>8–12</sup>

Indirect effects of COVID-19 mainly resulted from the overload of health systems globally, and from the consequences of the actions taken by governments to contain the spread of the virus. In Italy, in response to the outbreak of COVID-19, on 9 March 2020, the government imposed a nationwide lockdown, restricting the movement of the population, with exceptions for food supply, work and health circumstances. Further restrictive measures came into effect until the end of April 2020, which provided for the suspension of all activities not deemed necessary. During the second (October 2020–May 2021) and third (from October 2021 on) pandemic waves, mitigation strategies were again adopted, with the primary aim to limit the congestion of health services, also put under pressure by shortage of health personnel.

Hospital saturation characterised all three pandemic waves in Italy, forcing the cancellation and postponement of non-urgent procedures. Regional health services were reorganised, with reprioritisation of routine care and redefinition of essential interventions. In addition, general concerns about contracting the virus drove most patients to defer basic treatment, compromising continuity of care.

Many studies have reported changes in healthcare utilisation for non-COVID-19 conditions.<sup>9 13–17</sup> Decreased hospital admission rates and increased mortality rates were reported for time-dependent diseases such as acute myocardial infarction<sup>18–21</sup> and stroke.<sup>22 23</sup> Some evidence also emerged of a substantial disruption in the standard care of chronic diseases: delayed or missed diagnoses and treatment were observed across many countries<sup>24</sup>; emergency visits and hospitalisations significantly decreased especially during the first COVID-19 wave,<sup>25–28</sup> putting patients with chronic disease at higher risk of increased morbidity and mortality. To date, however, there are still few studies that have thoroughly investigated the indirect effects of COVID-19 on patients with chronic disease, measuring the variation in the access to different health services and for a period longer than the first pandemic wave.

With the present study, we aimed to explore and quantify this variation during a 2-year pandemic period, including 2020 and 2021. We focused our research on a region-wide scale, considering the prevalent chronic disease population residing in the Emilia-Romagna Region (ERR), one of the most affected Italian areas since the beginning of the pandemic, with over 19 100 deaths in a resident population of approximately 4 460 000 people. In addition, ERR has developed an efficient information system, based on various healthcare administrative databases, which we used to accurately estimate

the trend in the number of deaths among people with pre-existing medical conditions, as well as their access to both inpatient and outpatient healthcare resources during 2020 and 2021.

## METHODS

### Study design and population

This is a population-based retrospective study, resulting from the monitoring carried out by the ERR Health Department to support health policy decision-makers in the management of healthcare services and resources. Ethical review and approval were waived for this study in accordance with the ERR Regulation, which states that anonymised administrative data can be used for relevant public interest objectives, that is, for healthcare planning, management, quality evaluation and improvement.

The study population was composed of adults residing in the ERR in the period January 2020–December 2021, affected by at least 1 of 32 chronic conditions considered. Each year a different cohort was identified, consisting of chronic disease cases identified in the previous year and still alive, in addition to new cases. New cases consisted of both patients who did not have any chronic conditions in the previous year and patients suffering from other pre-existing chronic pathologies. To assess the indirect impact of the pandemic waves, similar reference populations were selected in the previous 3-year period 2017–2019, considering the chronic disease cases prevalent during each year.

### Data sources and patient selection criteria

The present study used data derived from 15 different regional health databases (online supplemental table 1). Based on a previous scoping review exploring the epidemiology of multimorbidity and its impact on the healthcare system,<sup>29</sup> we identified 32 prevalent chronic diseases, that may be seriously disabling or life-threatening for the patient and require significant dedicated healthcare resources. Patients with at least one of these chronic conditions were selected based on the anonymous identifier assigned by the region. Among these patients with chronic disease, those with a positive SARS-CoV-2 molecular test were identified through the regional database DB-COVID-19, established for monitoring the pandemic and still active. The date of positive diagnosis was also recorded. A summary of the data sources used is detailed in online supplemental table 2; ICD9-CM diagnosis codes, ATC drug codes and exemption codes used to trace individual conditions are displayed in online supplemental table 3.

### Endpoints and statistical analysis

The effects of the indirect impact of COVID-19 on patients with chronic disease was addressed by considering the following endpoints:

### Non-COVID-19 deaths

The number of patients with chronic disease who died for causes (either primary or secondary) other than COVID-19 in the period 2017–2021 was identified among the patients with chronic disease prevalent in each year, through record-linkage with the Regional Mortality Register (REM).

According to the directives of the Italian National Institute of Health, the REM registration of patients who died from COVID-19 had to follow the guidelines provided by the European Centre for Disease Prevention and Control and the WHO.<sup>30</sup>

### Non-COVID-19 hospitalisations

The number of patients with chronic disease hospitalised during the 2-year pandemic period was calculated based on the hospital discharge database (SDO). COVID-19-related hospitalisations were excluded from the analysis.

### End-of-life healthcare

Assistance of patients with chronic disease in the last month of life was explored through record-linkage with the following data sources: SDO, OSCO, Hospice, SDRES, CRA and ADI. We compared the amount and type of end-of-life care received by patients with chronic disease either including or excluding COVID-19 cases.

### Major procedures

Major procedures were analysed based on information acquired from SDO, excluding COVID-19-related hospitalisations. They were defined according to the Agency for Healthcare Research and Quality classification.<sup>31</sup>

### Emergency care

The trend in the access to the emergency room (ER) was analysed both overall and separately for high/medium versus low severity cases.

### Homecare

Social and healthcare provided by various professionals (as doctors, social and health workers (OSS), physiotherapists, pharmacists, psychologists, etc) to patients with chronic disease within their home, was evaluated through record-linkage with the ADI database.

### Outpatient care

The trend in the number of diagnostic and lab tests, rehabilitation therapies, therapeutic procedures and specialist visits for patients without COVID-19 chronic disease were analysed based on information derived from ASA data source.

The above endpoints were explored during the two pandemic years considered (2020 and 2021) and compared with the expected numbers estimated from the pre-pandemic period 2017–2019. In the event of positive SARS-CoV-2 cases, all healthcare episodes that occurred in the 30 days following the date of COVID-19 diagnosis were excluded from the analyses.

For each type of care, a descriptive analysis of the trend was first performed from 1 January 2017 to 31 December 2021 to assess the seasonal and cyclical components. Next, an interrupted time series analysis was carried out using Poisson or negative binomial models, having as covariates the time trend, the seasonal component expressed by sine and cosine functions of the trend, the days of the week and the months.<sup>32–34</sup> The residual autocorrelation was checked through Ljung-Box test.<sup>35</sup> To estimate the expected number of healthcare services based on the trend of the 3-year pre-pandemic period, a Poisson or negative binomial model was used for the 2017–2019 data related to each type of assistance, having as a dependent variable the number of services and as covariates the time and the seasonal and cyclical components. The resulting parameters were applied to the 2020 and 2021 data. These estimates are reported only graphically.

The incident rate ratio (IRR) between the number of delivered versus expected healthcare services was estimated using, as a reference, the daily number of living patients with chronic disease, not infected with SARS-CoV-2 (thereafter, referred to as patients without COVID-19 chronic disease), and weighted by age, gender and number of concomitant pathologies. Therefore, for each type of treatment and for each month, a Poisson regression model was applied having the logarithm of the daily number of patients without COVID-19 chronic disease as offset, the year expressed as a dichotomous variable (2020 or 2021), and age groups, gender and number of co-occurring diseases as covariates.<sup>33</sup> The IRR for each type of assistance and for each month was obtained from the exponential of the coefficient estimated for the dichotomous variable indicating the year. Positive or negative IRR values, respectively, indicate an excess or a reduction, compared with the same months of the pre-pandemic period. Variations recorded in the pandemic versus pre-pandemic period are expressed in percentages by the complement of 1 of the IRR:  $(IRR-1) * 100$ . The health episodes that occurred in 2020 were excluded from the model for the 2021 IRR estimates to maintain the 2017–2019 3-year period as the reference time for all estimates.

Variations in mortality recorded in the period 2020–2021, with respect to the period 2017–2019, were calculated monthly, estimating a logistic model relating to the 2017–2019 data and subsequently applying the estimated coefficients to the 2020–2021 population (using the *inmodel* statement within the SAS logistic procedure). The risk factors included as covariates in the model were age, gender, number and type of chronic diseases. The expected number of deaths for 2020 and 2021 was obtained from the sum of the probabilities estimated by the model for each patient. The ratio between the number of observed versus expected (O/E) deaths in 2020 and 2021 was calculated to estimate the excess mortality that occurred monthly. Values above 1 indicate an increase in mortality, while values below 1 indicate a reduction in mortality. The 95% CI was obtained by multiplying the

SE of O/E ratios by 1.96. O/E ratios with 95% CI not containing the value 1 were considered statistically significant. A similar method was used to analyse end-of-life healthcare throughout the months of the pandemic.

All analyses were performed using R V.3.6.3 (The R Foundation for Statistical Computing, Wien) and SAS V.9.3 (SAS Institute).

### Patient and public involvement

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

## RESULTS

In 2020, chronic disease prevalence in the ERR was 47.7% in the overall adult population, corresponding to 1 791 189 patients diagnosed with one to multiple chronic conditions. Similarly, in 2021, patients with chronic disease were 1 801 071, 47.8% of the total resident adults. The demographic and clinical characteristics of the ERR chronic disease population are shown in [table 1](#).

### Non-COVID-19 deaths

Overall, non-COVID-19 deaths among patients with chronic disease in the 2020–2021 period were 93 370, with annual numbers (47867 in 2020 and 45511 in 2021) that did not differ significantly from those of the previous 3 years (2017: 47 707; 2018: 46 775; 2019: 47 306). However, the trend showed an excess of observed versus expected deaths in the first months of 2020, with the pandemic breakout and the consequent lockdown measure ([figure 1A](#)). Then, the number of deaths decreased considerably until returning to the expected mortality levels, comparable to those recorded in the summer period of the prepandemic years. The second pandemic wave resulted in a mortality increase in October 2020, followed by a number of deaths that, in the subsequent months, remained well below that recorded in the same months of the previous reference period.

Overall, in the 24 months considered, non-COVID-19 mortality among patients with chronic disease was 2.7%, slightly though significantly higher than the expected mortality (2.5%), estimated based on the clinical complexity of the patients under study (observed/expected: 1.06, 95% CI 1.05 to 1.07).

A higher-than-expected mortality (adjusted for the clinical and demographic characteristics of the patients) was observed from February to December 2020 (except for May) ([figure 1B](#)). Particularly marked was the increase recorded in March 2020 (+35%), followed by a sharp reduction in May 2020, with observed mortality below the expected values (−3%), and a subsequent increase until October 2020 (+13%). Non-COVID-19 deaths were significantly lower than expected in the first 4 months of 2021 and then increased again, although in a moderate way, through the end of 2021.

### Healthcare of patients with chronic disease in the last month of life

Compared with the prepandemic period, hospitalisations decreased in the 2 years of the pandemic (2020–2021: 52% vs 2017–2019: 58.2%), whereas patients receiving home care (ADI), as well as those without any assistance traceable from the current health databases (home w/o ADI) increased (ADI: 17.6% vs 13.7%; home w/o ADI: 15.6% vs 13.4%) (online supplemental table 4).

After adjusting for the characteristics of patients with chronic disease, including age, gender, number and type of concomitant diseases, hospice admissions (including both COVID-19 and non-COVID-19 cases) increased by 21% in the pandemic period compared with the period 2017–2019, while hospitalisations decreased (−4%) (online supplemental figure 1). Notably, hospitalisations of patients without COVID-19 chronic disease decreased significantly (−19%), while home care, with and w/o ADI, increased by 7% and 9%, respectively. Healthcare based on Hospice, OSCO, SDRES and CRA were comparable over the years.

### Healthcare of patients without COVID-19 chronic disease during the pandemic period

We compared the trend of observed versus expected access of patients without COVID-19 chronic disease to different health services in the period 2017–2021 ([figure 2](#)).

*Hospitalisations.* Hospitalisations followed a constant seasonal trend over the years, with marked reductions in correspondence with Christmas holidays, subsequent peaks between mid-January and February and then a decrease in the following months characterised by a negative peak in the month of August. In 2020, in correspondence with the lockdown restrictive measure, on 9 March 2020, a rapid and substantial decrease in hospitalisations, which continued until May, was observed. In this period, relevant reductions (March: −29.7%; April: −42.7%; May: −39.2%) were recorded. Since the beginning of June, with the attenuation of the spread of the virus, the daily number of hospitalisations increased again, though remaining below the expected trend. The second and third pandemic waves imposed new containment measures and therefore a reduction in hospitalisations was observed. This trend became significant from November onwards, with percentages fluctuating between −13.5% and −25.3%. Overall, in 2020 and 2021, there was a 15.5% decrease in hospitalisations for causes other than COVID-19, compared with the prepandemic period ([table 2](#)). The monthly percentage change in hospitalisations of patients without COVID-19 chronic disease in 2020 and 2021 compared with the pre-COVID-19 period is detailed in online supplemental table 5.

### Major procedures

We observed a significant reduction in the first 3 months of the pandemic (−40.5%, −50.1% and −40.5% respectively), mainly due to the postponement of planned interventions, as established at ministerial level. Subsequently,

**Table 1** Characteristics of the regional chronic disease population (years 2020 and 2021)

Demographic and clinical characteristics	2020		2021		
	Prevalence		Prevalence		
	N	%	N	%	
Sex					
	F	988 651	55.2	994 421	55.2
	M	802 538	44.8	806 650	44.8
Age					
	18–40	172 678	9.6	173 375	9.6
	41–50	210 098	11.7	206 607	11.5
	51–60	327 912	18.3	335 657	18.6
	61–70	367 005	20.5	371 983	20.7
	71–80	383 154	21.4	381 495	21.2
	>80	330 342	18.4	331 954	18.4
Chronic disease					
	Hyperlipidaemia	578 226	15.4	606 907	16.1
	Hypertension	399 998	10.6	387 178	10.3
	Rheumatological conditions	369 223	9.8	358 503	9.5
	Thyroid pathology	323 003	8.6	331 700	8.8
	Neoplasms	286 051	7.6	295 421	7.8
	Depression	283 753	7.5	284 859	7.6
	Diabetes mellitus	282 221	7.5	287 602	7.6
	Prostatic hyperplasia	178 728	4.8	178 987	4.8
	Gout	139 673	3.7	141 946	3.8
	COPD	139 387	3.7	127 557	3.4
	Reduced vision	134 820	3.6	133 953	3.6
	Cardiac arrhythmias	121 187	3.2	118 243	3.1
	Ischaemic heart disease	118 133	3.1	114 678	3
	Gastro-oesophageal pathology	114 449	3.0	116 179	3.1
	Epilepsy	100 737	2.7	105 194	2.8
	Osteoporosis, Paget	92 582	2.5	88 605	2.4
	Psychosis, schizophrenia, bipolar disorder	77 638	2.1	77 871	2.1
	Cerebrovascular disease	73 130	1.9	68 302	1.8
	Congestive heart failure	69 663	1.9	66 993	1.8
	Other cardiovascular pathologies	66 343	1.8	62 440	1.7
	Dementia	65 098	1.7	61 038	1.6
	Asthma	42 754	1.1	45 889	1.2
	Chronic hepatitis	41 388	1.1	40 953	1.1
	Crohn, UC	36 279	1.0	37 259	1.0
	Parkinson	33 280	0.9	32 592	0.9
	Migraine	24 396	0.6	24 576	0.7
	Chronic renal failure	24 073	0.6	24 818	0.7
	Heart valves disease	21 085	0.6	20 486	0.5
	Cirrhosis	14 233	0.4	13 773	0.4
	Peripheral vascular disease	13 830	0.4	13 065	0.3
	Other neurological diseases	12 921	0.3	13 204	0.4
	Obesity	12 060	0.3	11 367	0.3

Continued

Table 1 Continued

Demographic and clinical characteristics	2020		2021	
	Prevalence		Prevalence	
	N	%	N	%
Hearing loss	5082	0.1	4675	0.1
Multimorbidity	1 039 678	27.7	1 046 717	27.8
1 disease	751 511	42.0	754 354	41.9
2 diseases	409 856	22.9	415 566	23.1
3 diseases	256 412	14.3	259 610	14.4
>3 diseases	373 410	20.9	371 541	20.6

COPD, chronic obstructive pulmonary disease; UC, ulcerative colitis.

the observed trend increased to almost overlap that expected in the following months. With the second and third pandemic waves, the number of major procedures decreased again. Compared with the 2017–2019, in the 24 months considered, the total reduction was –19.6%. Monthly percentage changes are reported in online supplemental table 5.

#### Access to ER

ER utilisation collapsed by about 40% since the beginning of the health emergency decreed by the Italian government, on 22 February 2020. Compared with the previous 3 years, in the 24 months of the pandemic, the reduction was –23.7%. In addition, the trend did not change even when considering critical (high) and urgent (medium) severity cases (online supplemental figure 2A). Especially in the first 2 months of the lockdown, there was an unprecedented collapse of accesses for high and medium severity cases (–31.6% in March and –38.0% in April). Their overall reduction was –26.3%, whereas accesses for low-severity cases (ie, non-urgent or deferrable conditions), representing two-thirds of the total number of ER visits, decreased by 23.2% (online supplemental table 4 and figure 2B).

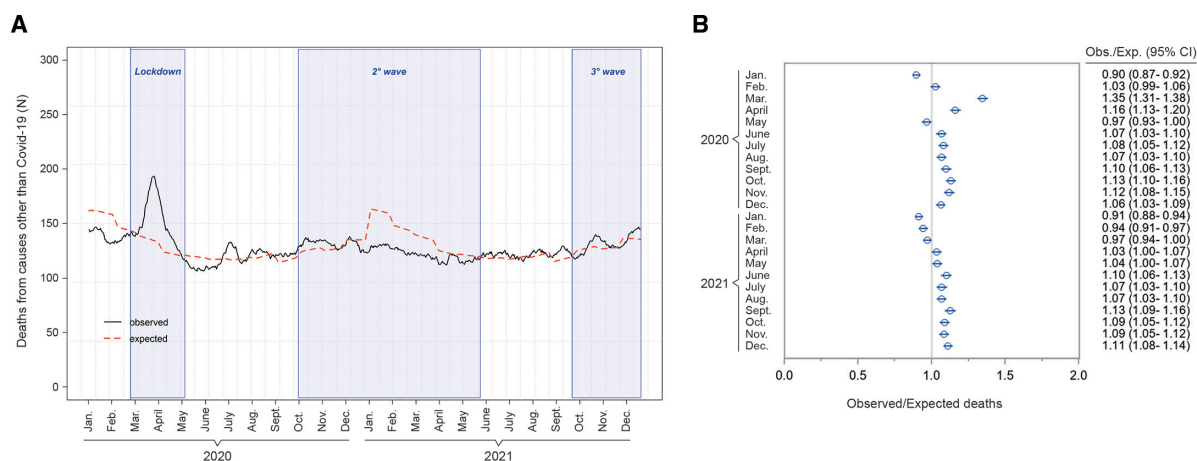
#### Homecare (ADI)

Homecare was less affected than other forms of assistance, decreasing, on average, by 9.8%. The most sudden drops were observed during the first lockdown (May: –18.1%), and just as the second pandemic wave reached its peak (January 2021: –13.9%). A significant decrease was also observed at the end of 2021 (see online supplemental table 4 for monthly percentage changes).

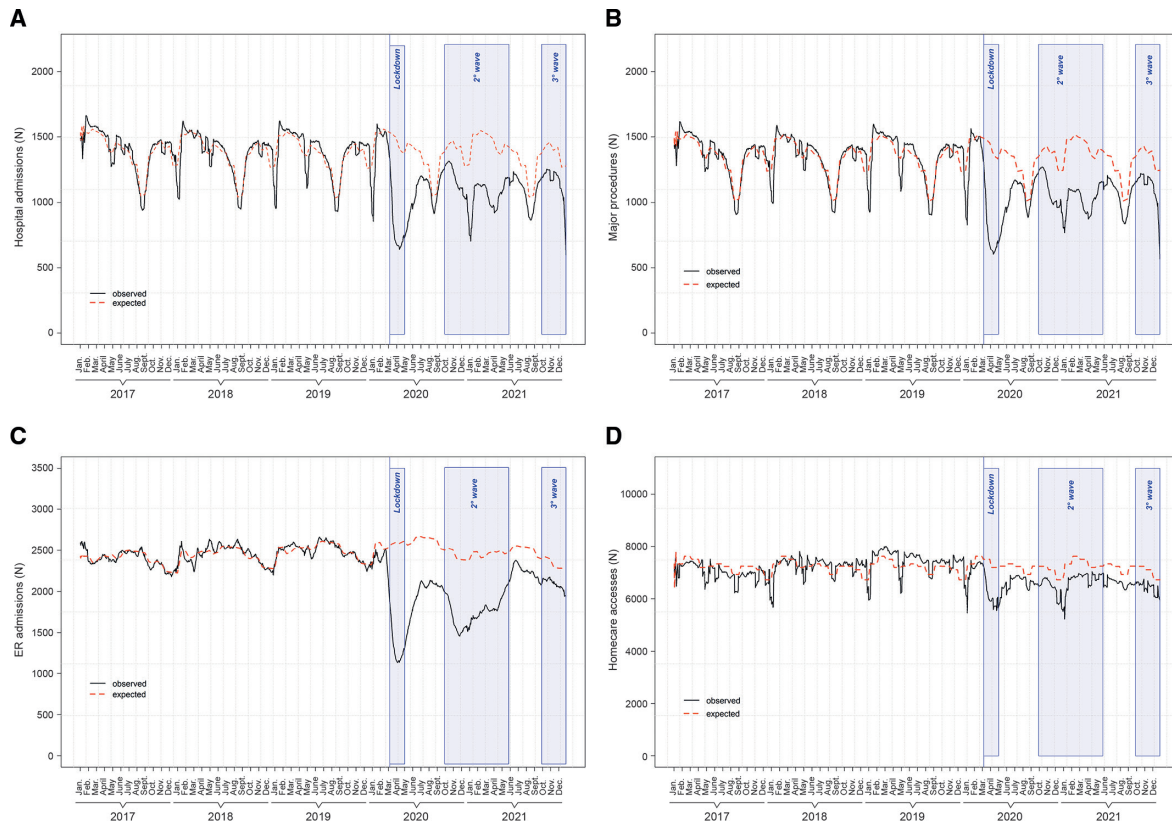
#### Outpatient care of patients without COVID-19 chronic disease during the pandemic period

The pandemic strongly impacted on outpatient care. Since the first days of the lockdown, non-urgent outpatient activities were suspended, in compliance with the ministerial directives. In the months following the lockdown, there was a slow recovery of outpatient care although it remained at levels significantly lower than those expected. Figure 3 shows the observed/expected trend in the access of patients with chronic disease to different types of outpatient care in the period 2017–2021.

Statistically significant reductions ranging between –60% and –80% were recorded for most of outpatient care from March to May 2020. In the following months,



**Figure 1** Observed and expected trend in the number of deaths of patients with chronic disease, excluding COVID-19 cases. (A) Monthly observed/expected death ratio (95% CI). (B) Observed period: 2020–2021; reference period: 2017–2019.



**Figure 2** Trend in hospitalisations: (A) major procedures, (B) emergency room accesses, (C) and homecare, (D) for patients without COVID-19 chronic disease (period 2017–2021).

the accesses still settled below the average of the pre-COVID-19 period, even if the difference was much more attenuated. Specialist visits and diagnostic tests were overall the most affected,  $-22.3\%$  and  $-16.6\%$ , respectively; more contained, below  $-10\%$ , was the reduction in the provision of therapeutic procedures and rehabilitation therapies (see also online supplemental table 6).

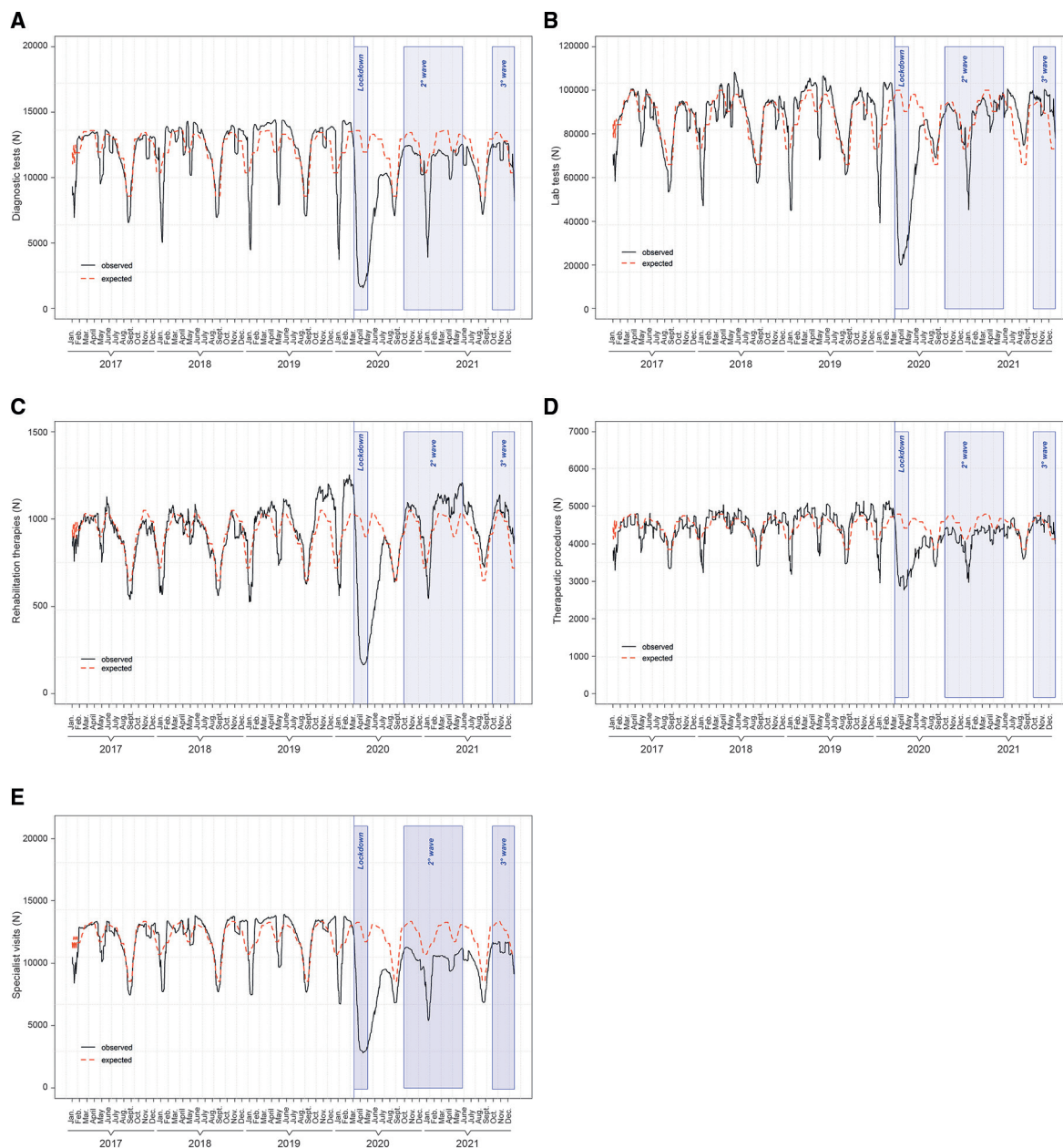
### DISCUSSION

People suffering from chronic diseases need continuous access to healthcare services to carry out routine or specialist visits, and control tests. The COVID-19 pandemic has placed significant demands on the healthcare systems, which inevitably diverted resources away from routine care, thus preventing many patients without

**Table 2** Overall change in the access of patients without COVID-19 chronic disease to the different healthcare services in the 2020–2021 pandemic period, compared with the baseline prepandemic period 2017–2019

Type of healthcare service	Period 2020–2021			
	N	(IRR-1) %	95% CI	P value
Hospitalisations	837 594	-15.5	(-15.7 to -15.3)	< 0.0001
Major procedures	774 329	-19.6	(-19.8 to -19.4)	<0.0001
Access to emergency room	1 364 726	-23.7	(-23.9 to -23.5)	<0.0001
High/medium severity cases	379 778	-26.3	(-26.6 to -26.0)	<0.0001
Low severity cases	937 526	-23.2	(-23.4 to -23.1)	<0.0001
Homecare	4 807 956	-9.8	(-9.9 to -9.7)	<0.0001
Diagnostic tests	7 461 528	-16.6	(-16.6 to -16.5)	<0.0001
Lab tests	60 135 758	-6.4	(-6.4 to -6.4)	<0.0001
Rehabilitation therapies	656 485	-2.5	(-2.8 to -2.2)	<0.0001
Therapeutic procedures	3 032 973	-7.4	(-7.5 to -7.2)	<0.0001
Specialist visits	6 878 937	-22.3	(-22.3 to -22.2)	<0.0001

IRR, incidence rate ratio.



**Figure 3** Trend in diagnostic tests: (A) lab tests, (B) rehabilitation therapies, (C) therapeutic procedures, (D) and specialist visits (E) for patients without COVID-19 chronic disease (period 2017–2021).

COVID-19 chronic disease from undergoing proper follow-up.

This study tackled this issue in a region of over 4 million inhabitants, highly representative of the pandemic crisis in Italy, the first European country to experience the harming impact of SARS-CoV-2 infection. To the best of our knowledge, this is the most updated and comprehensive subnational report about the indirect pandemic consequences on a large and well-defined chronic disease population.

The trend in non-COVID-19 excess mortality among the patients with chronic disease under study showed an initial phase, corresponding to the first pandemic wave and the adoption of a national lockdown, characterised by a significant non-COVID-19 excess mortality. A second

phase, including both the second and third pandemic waves, was marked by much less disruptive variations in non-COVID-19 deaths, which remained around or even below the excess mortality threshold. Similar trends in cause-specific and all-cause mortality were reported both at the subnational and national level in several European countries<sup>36–39</sup> and worldwide.<sup>7 40</sup> As already suggested,<sup>36 38</sup> non-COVID-19 excess mortality may, to some extent, indicate under-reporting or underdiagnosis of COVID-19, especially during the first pandemic phase, when the clinical presentation of the disease was still under investigation and testing rates were low. However, the increase in mortality, particularly for some chronic conditions, was also related to reduced access to healthcare resources due to their redirection towards assistance of patients



with COVID-19 and the fear of contracting the virus. It has been pointed out that it is difficult to distinguish the specific contribution of COVID-19 underdiagnosis from the overburdening of health systems.<sup>36 38</sup> In Italy, the rapid increase in SARS-CoV-2 cases and all-cause mortality recorded in the first months of 2020 mainly involved the northern regions, including ERR, where healthcare services are known to be highly performing, and yet they were equally overwhelmed. Indeed, our results showed that from March to May 2020, there was a sharp decline in patient with chronic disease access to many regional healthcare services, which most likely contributed to the worsening of the disease or death of many with pre-existing medical conditions. The reduction in non-COVID-19 mortality observed after the first lockdown may also indicate both a recovery in health services and an improvement in the ability to detect COVID-19 cases. However, it could also be partly explained by the high mortality of elderly and more vulnerable patients during the first wave,<sup>41 42</sup> which effectively reduced the population at higher risk of death in the subsequent pandemic phases. Moreover, additional policy interventions were introduced, including greater hand hygiene, the wearing of masks, physical distancing and closure of public spaces, which may have reinforced the mitigating effect of the lockdown already in place.

The access of patients without COVID-19 chronic disease to different ERR healthcare services, such as hospitalisations, major procedures and ER visits halved during the first wave and were evident signs of the pandemic crisis. These results confirm and complement those reported by several studies since the beginning of the pandemic.<sup>5 16–18 43 44</sup> A recent systematic review about healthcare provision to patients without COVID-19 in Italy reported a decline in surgical activities in all fields and a reduction in urgent procedures due to a lack of ICU beds and fear of infection.<sup>45</sup> In support of this evidence, we found that home care of patients without COVID-19 chronic disease in the last 30 days of life significantly increased compared with the prepandemic period, indicating a clear paradigm shift in the way prioritisation of care was handled. Indeed, the pandemic has presented a unique challenge for end-of-life healthcare providers, forced to ration services in favour of patients who had the best chance of survival.<sup>46 47</sup> A recent study in a large region of northern Italy provided evidence for a significantly reduced hospital care of older chronic disease patients; however, this reduction was greater for non-chronic disease patients, suggesting that there has been some attempt to scale up healthcare of more vulnerable patients.<sup>28</sup> Our findings are consistent with this observation, as the dramatic decline in hospitalisations, as well as ER visits and major procedures for patients with chronic disease during the first outbreak, markedly recovered over the course of 2020.

Prevention, early detection and ongoing patient monitoring are hallmarks of essential primary care, which is a key to encourage patients with chronic disease to be

adherent to the medications and manage their health conditions. During both 2020 and 2021, we observed disruption to ERR primary care for individuals with chronic illness, in terms of outpatient care delivery, due to government restrictions as well as instilled anxiety about potential COVID-19 exposure during in-person consultations. Specialist visits, diagnostic and lab tests, rehabilitation therapies and therapeutic procedures were particularly reduced (by up to 70%–80%) during the first pandemic wave. On the other hand, studies have shown that some outpatient services have been converted into telemedicine and online visits.<sup>14 48 49</sup>

It has been underlined that the delay or temporary cancellation of these services may have been safer than the risk of infection while using them.<sup>48</sup> The issue of too much medicine has also been raised, suggesting that reduced health services may have resulted in some people being spared unnecessary or potentially harmful care.<sup>15</sup> However, several patients with chronic disease may have missed essential care, with severe long-term health consequences. For example, newly diagnosed cancer conditions or patients undergoing cancer treatments were facing difficulty in getting constant follow-up or laboratory tests for better disease prognosis.<sup>50 51</sup> Cancer treatment delay was associated with an increase in mortality across all common forms of cancer treatment, with longer delays being progressively unfavourable.<sup>52</sup> Patients with mental and psychiatric diseases may have worsened their symptoms or not received their routine care because of diminished or less effective online psychotherapy sessions.<sup>8</sup> Similarly, chronic disease management has proven particularly challenging for people with diabetes, chronic obstructive pulmonary disease (COPD), hypertension, asthma and heart disease.<sup>14</sup> In addition, elderly patients, who represent a substantial subset of the chronic disease population, may have faced amplified fears and problems in maintaining their routine care. Indeed, recent surveys showed that health-related quality of life of many patients with chronic disease and their caregivers was substantially deteriorated during the pandemic.<sup>14 50 53</sup>

In Italy, successive guidelines were issued for the remodulation of both inpatient and outpatient activity, based on the assessment of the risk–benefit ratio and the incidence of cases in the local population.<sup>54</sup> The effects of these measures were reflected by the variation over time in the use of the various health services considered in this study. The drastic decline during the first wave was followed by a gradual safe reactivation of previously reduced or suspended activities, which were again reconfigured as soon as the epidemiological situation got worse. The causes of lack of access to health services have been recently reviewed<sup>55</sup>: the most frequent access barrier was the shortage of system resources, whereas predisposing (fear of infection, stigma, disinformation) and enabling (socioeconomic status and technology) barriers were the most reported in relation to public behaviour. Concern about seeking healthcare at a time when services were facing limitations was another factor influencing people

with chronic conditions to opt out of booking an outpatient or hospital visit in 2020.<sup>56</sup>

We acknowledge that our results have intrinsic limitations derived from the use of retrospective regional administrative data and we suggest caution in generalising them. Among these limitations, this study design did not allow an unambiguous interpretation of the causes of non-use of healthcare, nor did it allow a distinction between people who missed necessary care and those who avoided unnecessary care, which clearly had a different weight in assessing changes in healthcare utilisation. Moreover, administrative data did not allow to capture the increase in the healthcare needs of chronic disease patients caused by the interruption of routine care in the most critical phases of the pandemic or by any long-COVID-19 conditions. The assessment of the indirect impact of the pandemic carried out through this methodology was in fact inherently based on the assumption that, given the same clinical and demographic characteristics of patients, their healthcare needs were similar in the pre-pandemic and pandemic periods. Finally, possible errors in the reporting of COVID-19-related diagnoses or deaths, especially during the first phase of the pandemic when the clinical presentation of the disease was still being studied and testing rates were low or inconsistent, might have influenced the non-COVID-19 outcome estimates reported here. Likewise, the national COVID-19 vaccination campaign primarily aimed at people with pre-existing chronic conditions, certainly played an unquantifiable role in mitigating the mortality rate and underutilisation of health services as observed in 2021.

Nevertheless, our work provides an up-to-date and comprehensive picture of the indirect impact of 2 years of pandemic in terms of the access of a large non-COVID-19 chronic disease population to the different health services.

## CONCLUSION

We confirm that patients with chronic disease showed a substantial decrease in the utilisation of both inpatient and outpatient services, as well as end-of-life care. However, the overall non-COVID-19 excess mortality was contained, indicating that chronic disease care management was somehow able to counteract the indirect effects of the pandemic.

Although future research is needed to investigate how the pandemic impacted on the continuity of care for specific chronic diseases, these results are valuable for understanding health priorities that emerged under limited resource conditions and how the chronic disease population has been affected by changes and reorganisation in the healthcare system.

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## ORCID iD

Daniela Fortuna <http://orcid.org/0000-0003-0927-7199>

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