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Original Article/Research

The impact of health policies and vaccine rollout on the COVID-19 pandemic waves in Italy

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ABSTRACT

Background: Over the course of the COVID-19 pandemic in Italy, different response measures were taken to contain the spread of the virus. These include a variety of non-pharmaceutical interventions and a mass vaccination campaign. While not definitive, epidemiological measures provide some indication of the impact of such measures on the dynamics of the pandemic and lessons to better prepare for future emergencies.

Objective: To describe the impact of vaccine rollout and health policies on the evolution of the COVID-19 pandemic in Italy from March 2020 to October 2021 using a set of epidemiological indicators.

Methods: We performed a time-trend analysis of new confirmed COVID-19 cases, patients in hospital, and deaths. Using line charts, we informally assessed the relationship of these indicators with the immunization campaign and other health policies. Daily aggregate data were gathered from GitHub repositories of certified data from Italy's Government and Civil Protection.

Results: The immunization coverage increased starting in March 2021, with a parallel decrease in COVID-19 infections, hospitalizations, and deaths. Despite different implementation approaches, the vaccine coverage growth rate had a similar pattern across regions. A comprehensive approach including measures such as requiring face masks and a "Green Pass" to enter indoor places also helped contain the pandemic.

Conclusions: The vaccine rollout had a major effect on COVID-19 in Italy, especially on hospitalizations and deaths. Before the vaccine was available, however, other non-pharmaceutical interventions also helped to contain the spread of the virus and mitigate its effect on the population.

Introduction

The sudden and unexpected outbreak of coronavirus disease 2019 (COVID-19) in Italy caused severe health, social and economic consequences, including a huge strain on health services and on society as a whole [1–6]. Berardi et al. analyzed the policies implemented by the Italian government to counteract the spread of the virus during the first six months of the pandemic and their impact on health-related and non-health-related outcomes [7], highlighting how the strictness and timing of containment and prevention measures played a prominent role in curbing the consequences of the pandemic, both from a health and economic perspective. The authors also reported that, during the first pandemic wave, technological interventions played a marginal role due to the inadequacy of interventions' protocols and their delayed

implementation. Despite being comprehensive, the analysis of Berardi et al [7]. covered only a short time span in a very dynamic and rapidly evolving phenomenon. As the pandemic evolves, it is important to analyze the dynamic interplay between epidemiological indicators and the measures put in place accordingly to counteract the spread of the virus in order to examine the impact of the policies and technologies implemented and to draw lessons from the experience to be better prepared in case of future emergencies.

The event that surely represented the turning point for the COVID-19 pandemic worldwide was the development and deployment of COVID-19 vaccines at an unprecedented speed. The first clinical trial started 66 days after the publication on the net of the genomic sequence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [8]. Beyond the adoption of procedures to accelerate the process for

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emergency use authorization, such as the rolling review in Europe [9], the key element of this campaign was the deployment of different technologies, some of which have never been used in a licensed vaccine before.

However, before the beginning of the vaccination rollout, the trend of the indicators relating to the epidemic was associated with the adoption of health policies to preserve social distancing and reduce interactions at the national, regional and local level [10]. For instance, at the end of April 2020, a group of indicators for risk assessment were defined in order to gather aggregated data at a national, regional and local level. In particular, specific thresholds were set for the monitoring of these indicators, above which a national and regional joint assessment regarding the mitigation/containment measures was required in order to revise them or adopt new ones [11]. Moreover, starting from November 2020, a three-tiered restriction system was introduced on a regional basis. Tiers were assigned to each of the 21 regions and autonomous provinces of Italy following an epidemiological risk assessment provided by the Ministry of Health, based on the combination of 21 quantitative indicators. As reported by Manica et al [12], this three-tiered system of restrictions was associated with decreasing incidence and reduced effective reproductive number, thus allowing control of the pandemic also in terms of other epidemiological indicators (e.g. daily hospitalizations). Afterwards, with the progressive development of COVID-19 vaccines, national and regional governments more and more focused on the vaccination strategies, also considering logistical issues, such as distribution, allocation, infrastructure, human resources as well as communication campaigns [13]. In particular, when designing the vaccination program, the Italian Ministry of Health focused on the definition of subgroups of population at higher risk of COVID-19 hospitalization and death, by referring to a list of diseases (ICD-9-CM codes) that was shared with the regional governments to identify the priority groups for vaccination during the first phase of the campaign.

Many challenges were faced, such as the emergence, during the course of the pandemic, of new variants of SARS-CoV-2, potentially posing major issues in terms of clinical outcomes and vaccine effectiveness. Particularly, at the end of 2020, a variant that was significantly more transmissible than previously circulating variants, and subsequently named Alpha, was identified in the United Kingdom [14]. Shortly afterwards, different variants were identified across the globe such as in California, South Africa and India, named Beta, Gamma and Delta, respectively [8]. The biological evolution of this RNA virus has clearly changed the dynamics of the pandemic. New variants such as the one identified on November 9, 2021 in South Africa, namely Omicron, continue to emerge. Some of these could differ from the existing ones in terms of contagiousness, pathogenicity or immune-evasion, and rapidly become prevalent. Of note, in Italy, as of September 2021, 88.1% of the reported cases were due to the Delta variant, which progressively replaced the standard (Wuhan variant) and the Alpha variants [15].

In order to promote immunizations, Italy adopted a “Green Pass” in July 2021, and policies were developed for its implementation and use [16]. The Green Pass is a certification that proves that the holder has been fully vaccinated, recovered from COVID-19 or tested negative to a molecular or antigen test in the previous 48 h. With this certificate, people can have access to indoor restaurants, bars, theaters and other recreational venues. It is also needed to attend schools and universities. In summary, the Green Pass was implemented as a measure to encourage compliance with vaccination, increase the population’s immune coverage, and therefore reduce the circulation of the virus, allowing the “reopening” of the country.

Therefore, as strongly come to light during the COVID-19 pandemic, multiple foreseen (and especially unforeseen) events can occur in an emergency and drive the response against the threat it poses. A dynamic assessment is essential when looking at ever-evolving circumstances, which require specific measures and flexible solutions according to the epidemiological context. While not definitive, epidemiological measures provide some indication of the impact of such measures on the dynamics

of the pandemic and lessons to better prepare for future emergencies. Accordingly, the aim of this study is to describe the impact of vaccine rollout and other health policies on the evolution of the COVID-19 pandemic in Italy from March 2020 to October 2021 using a set of epidemiological indicators.

Methods

Data sources

We collected aggregate COVID-19 pandemic related data at the national and sub-national/regional level. Specifically, we gathered data on COVID-19 confirmed cases, deaths, patients in hospital, and testing from the Italian Civil Protection Department GitHub repository [17], and data on vaccinations rollout and coverage from the *Presidenza del Consiglio dei Ministri* GitHub repository [18]. Both repositories, which update their data daily, were accessed on October 11, 2021.

We obtained data on containment and closure policies, economic policies, health system policies and vaccination policies from the Oxford Covid-19 Government Response Tracker dataset [19].

Timeline of pandemic and policy interventions

In order to reflect changes in policy as well as the dynamics of the pandemic, we focused the analysis on four time periods: February 24, 2020 to June 11, 2020; October 14, 2020 to January 15, 2021; March 1, to May 15 2021,; and July 15, 2021 to October 10, 2021. These periods were chosen based on the shape of COVID-19 case curve and timing of policy changes by the Italian National Institute of Health [20,21]. We label these periods as the first to fourth “waves” to simplify the presentation of the descriptive analysis without judgements about complex epidemiological phenomenon underlying them [Table 1](#). identifies the national policy interventions that were implemented in Italy during the pandemic from the first wave onwards.

Analysis

In order to understand the interplay between the pandemic and the steps taken to control it, we performed a time-trend analysis of new COVID-19 confirmed cases, hospitalized patients and deaths. With the aid of line charts, we informally assessed the relationship of these indicators with Italy’s non-pharmaceutical interventions (policies) and mass immunization campaign (technology), measured as prevalence of fully vaccinated people. For each pandemic wave, we used and analyzed the epidemiological indicators reported in [Table S1](#) (Supplementary material).

Results: health policies, vaccination coverage, and epidemiological indicators

First wave: the full lockdown

The first COVID-19 patient in Italy was diagnosed on February 20, 2020, in Lombardy [22]. Following that, the virus rapidly spread, the number of cases quickly increased, and Northern Italy became extensively affected despite the implementation of local containment measures (e.g. red zones) [1–6]. The rapidly deteriorating situation led to the adoption of a full lockdown on March 10, 2020, when there were 10, 149 confirmed cases and 631 deaths [23]. Berardi et al [7]. reported that, nationally, the peak of contagion occurred on March 21, 2020, with approximately 11 cases per 100,000 population. April 26, 2020 marked the first day with more recoveries than new cases, almost two months since the start of the national lockdown.

At the end of April 2020, a group of indicators related to monitoring and diagnostic capacity, identification and management of cases and resilience of regional healthcare systems were established [24]. These

Table 1

Timeline of main policy interventions and Italian Legislative Decrees during the different pandemic waves.

Date	Description	Pandemic wave
March 8, 2020	Legislative Decree March 8, 2020: beginning of full national lockdown	First wave
May 18, 2020	End of full national lockdown.	
October 13, and November 6, 2020	Legislative Decrees introducing restrictions at the regional level, defining the “three-color system”: restrictions enacted based on epidemiological risk assessment performed by the Ministry of Health.	Second wave
December 3, 2020	Legislative Decree establishing stricter measures from December 21, 2020 to January 6, 2021. Specifically, the Decree introduces travel restrictions, quarantine for Italians returning from abroad, closure of ski resorts, and suspension of sea cruises.	
December 27, 2020	Beginning of the vaccination campaign against COVID-19 across Europe.	Third wave
January 2, 2021	Legislative Decree defining the preparation and implementation of the vaccination strategy in Italy.	
January 13, 2021	Decree introducing the ban on travel between regions until February 15, 2021, and the white area (“low” risk level and an incidence of infections, for three consecutive weeks, of less than 50 cases per 100,000 population). With subsequent Decrees, the ban on travel between regions is extended until March 27, 2021.	
March 10, 2021	Interim recommendations on target populations of the vaccination strategy (updated categories of people to be vaccinated and priorities).	
March 13, 2021	COVID-19 vaccination plan for the general population (second phase of the vaccination campaign).	Fourth wave
April 22, 2021	Legislative Decree defining the time schedule for the progressive elimination of the restrictions to limit SARS-CoV-2 infections, considering the scientific data on the epidemic and the progress of the vaccination campaign.	
May 17, 2021	Decree modifying the entry parameters for the “three-color system”, according to criteria proposed by the Ministry of Health.	
July 23, 2021	Decree defining the methods of use of the Green Pass and new criteria/entry parameters for the “three-color system”.	

indicators (see Table S2 Supplementary material for details) [cita] were used to progressively lift the containment measures in each region. Once a decreasing trend was confirmed, the national government gradually loosened the lockdown starting from May 4, 2020. This date is considered the end of the first pandemic wave. After the easing of the containment measures, a national lockdown was never put back again in place, although during the summer of 2020 the virus widely spread within the country, especially due to the higher mobility during the holiday season [5].

The first wave of the pandemic in Italy was characterized by a strong exponential growth and an equally marked decrease of the epidemic curve, due to the full national lockdown [1–7]. The first wave took the healthcare system by surprise, since the system was not prepared to face such a threat and lacked diagnostic capacity [1]. This is reflected in the period-specific case-fatality rates (CFRs) of each pandemic wave: 14.5%, 2.2%, 2.1% and 0.8%, respectively (Fig. 1). Specifically, during the first wave, Italy had one of the highest CFR among the countries that reported COVID-19 data [25], reaching a value resembling the one attributed to the 2002–2004 SARS epidemic (11%) [26].

Second wave: the three-color tier system

Starting at the end of September 2020, the Italian government progressively increased restrictions aimed at promoting physical distancing to contain the spreading of SARS-CoV-2 infections [12]. As reported by Berardi et al., the measures adopted by the government included the mandatory use of face masks in outdoor settings and the reduction of opening hours and capacity for restaurants, bars, theaters, and other recreational venues [13].

In October 2020, the Italian plan, “Prevention and response to COVID-19: evolution of strategy and planning in the transition phase for the autumn-winter season,” was published [27]. In particular, the document drew on the analysis of the critical issues that emerged in Italy during the first phase of the pandemic, aiming at providing support for the assessment and enhancement of health system preparedness at the regional level, taking into account a possible increase in SARS-CoV-2 infections and different potential scenarios for the autumn-winter season. The plan also describes the steps taken to implement an integrated surveillance system using different data sources.

On November 6, 2020, the national government introduced a “three-color system” (three increasing tiers of restrictions) to enact restrictions in each of Italy’s 21 autonomous regions based on 21 epidemiological indicators. This was the scenario in Italy at the beginning of the second wave of the pandemic, with a rapidly increasing number of confirmed cases and deaths (Fig 2, Fig 4).

The low prevalence of disease-induced immunization in the Italian population and the lack of approved treatments and vaccines [28,29] led to a high number of cases, hospitalization and deaths, albeit with a lower CFR (2.2%). This high number of confirmed cases and deaths can be explained by the looseness of containment measures during summer 2020 accompanied by improved tracing and testing capacity in almost all Italian regions, which allowed to track a higher number of cases as compared to the first pandemic wave [1-6, 24]. Moreover, on January 8, 2021, the Italian government introduced rapid antigen-tests for SARS-CoV-2 to the laboratory criterion for COVID-19 case definition [30]. The inclusion of these tests contributed to the reduction in the daily positivity rate (Figure S1), which has since dropped dramatically and never exceeded 7–8%. Furthermore, the start of the academic/school year in mid-September 2020 and the resumption of working activities after summer possibly contributed to the spread of the virus. Notably, once containment measures were re-introduced in November 2020, the number of cases started to decline after two weeks (Fig. 2), similar to the lag time usually reported in the available literature [1–8].

In mid-January 2021 the second pandemic wave came to a degrowth phase. A few days earlier, on December 27, 2020, in Italy as well as across Europe, the first dose of COVID-19 vaccine was administered.

Third wave: similar epidemiological trend, better outcomes

A few weeks after the vaccination campaign started, cases, hospitalizations and deaths increased (Fig. 2-4). It was the beginning of the third pandemic wave (March 1 to May 15, 2021). At that time, the number of eligible people who had received the second dose was less than 10%. There were both differences and similarities in the pattern of the epidemiological indicators between the second and third pandemic waves. Specifically, while the number of cases was lower in the third wave (40 cases per 100,000) as compared to the second wave (60 cases per 100,000), the number of patients in hospital was similar (Fig. 3). In the fall of 2020 the healthcare system was still not completely prepared to withstand the blow of the second wave, with hospital admissions mainly concerning higher-risk/severe patients [5]. H, when the third pandemic wave struck, the higher number of COVID-19 reserved beds and intensive care unit (ICU) beds led to the admission of patients with less severe forms of COVID-19. Bed occupancy was still high, but the quality of care provided was higher [31] as evidenced by better health outcomes, including fewer deaths. Increases in the number of ordinary

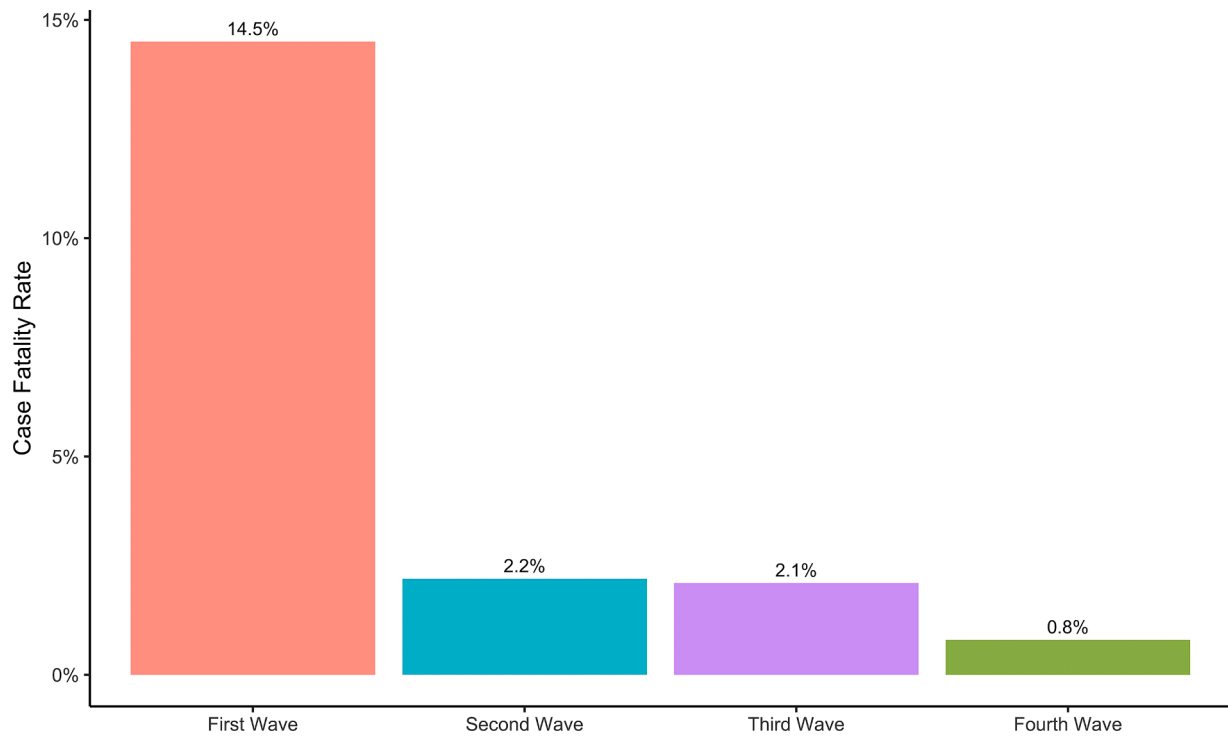


Fig. 1. Period-specific case-fatality rate. First wave: February 24, 2020 to June 11, 2020; second wave: October 14, 2020 to January 15, 2021; third wave: March 1 to May 15, 2021; fourth wave: July 15, 2021 to current date (October 10, 2021).

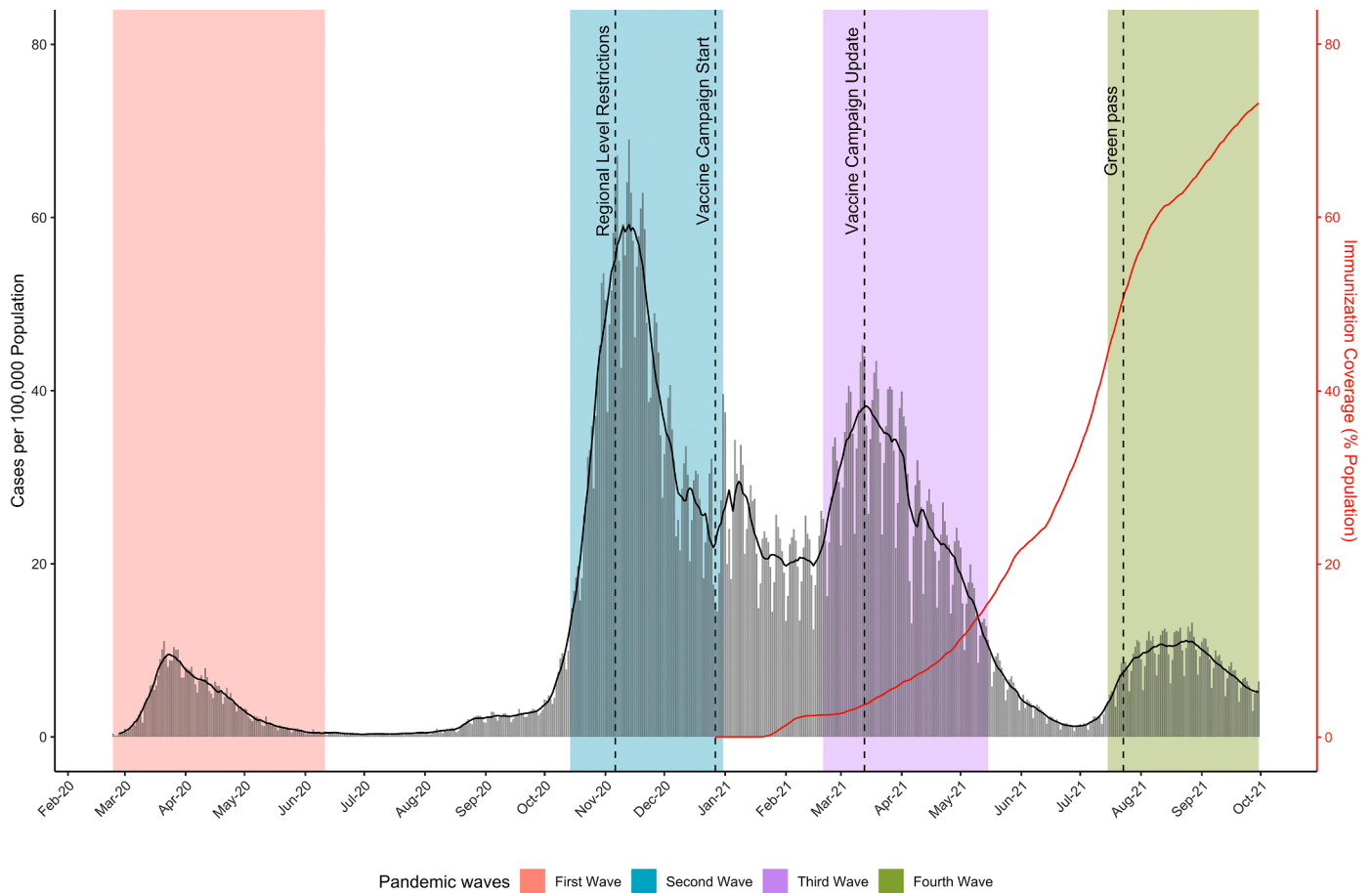


Fig. 2. Health policy measures, population immunization coverage, and COVID-19 incidence in Italy (per 100,000 population).

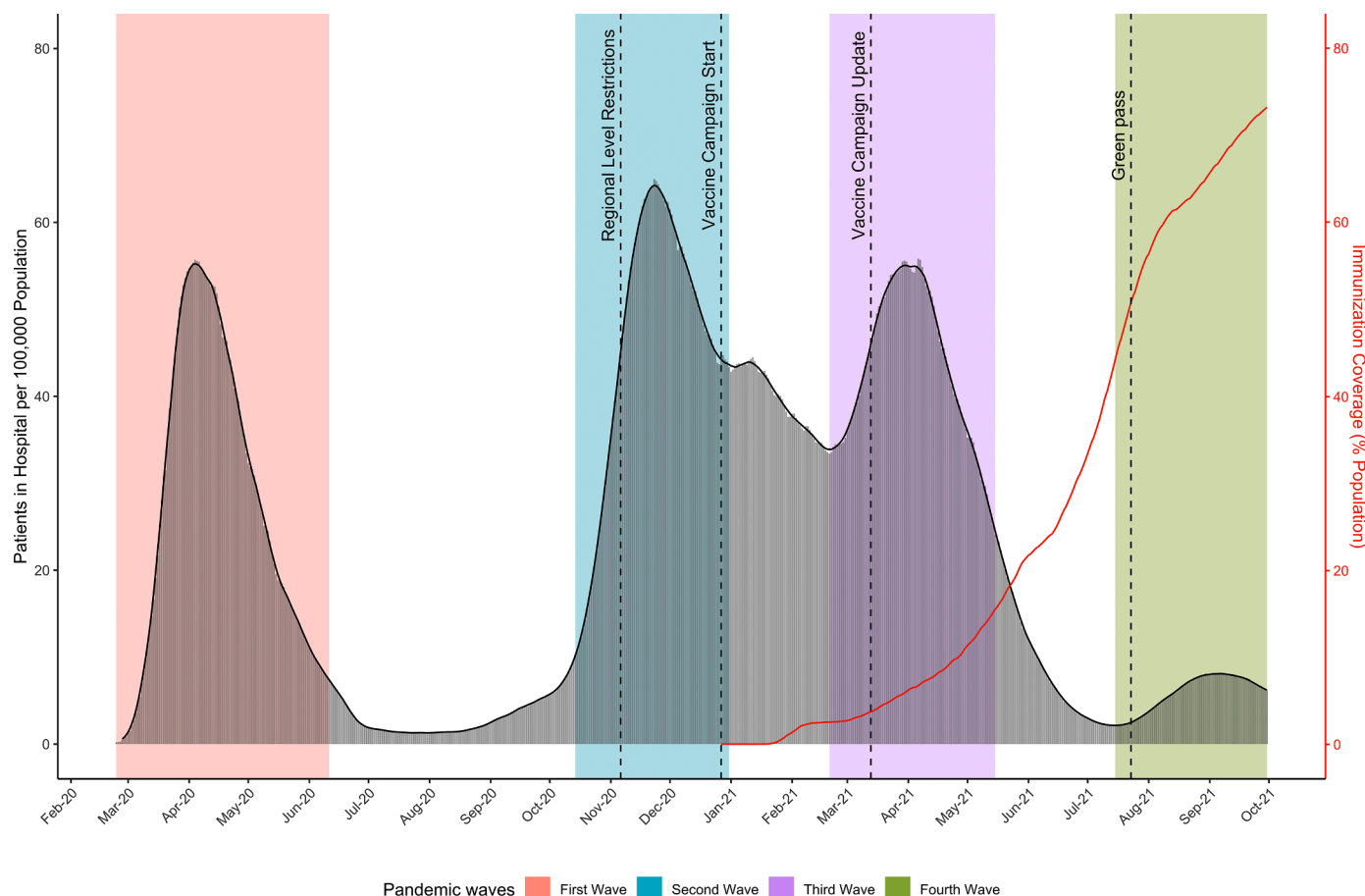


Fig. 3. Health policy measures, population immunization coverage, and COVID-19 patients in hospital in Italy (per 100,000 population).

and ICU beds and improved clinical management, paired with timely health policy measures (social distancing, regional closures, etc.) and the beginning of the vaccine campaign, are likely to be responsible for the reduction in the number of cases and deaths. Nevertheless, the effect of the vaccination coverage for the eligible population during the third pandemic wave was undermined by the small number of people with complete immunization. The only subpopulations with a high percentage of complete immunization were healthcare professionals and long-term care facility (LTCFs) residents [32]. In fact, these two populations were less likely to die or be hospitalized than the general population. Specifically, in the subpopulation that received the COVID-19 vaccine during the first campaign phase (January-March 2020), COVID-19 incidence dropped from 2.90 cases per 10,000 person-days to 1.33 per 10,000 person-days [33]. Hospital admission incidence dropped from 0.44 to 0.18 per 10,000 person-days [33] and mortality rate dropped from 0.18 to 0.04 per 10,000 person-days.

Consistently, data from the vaccine surveillance system showed that, as vaccination coverage increased, a reduction was observed in deaths from COVID-19 among healthcare workers, among LTCF elderly, and in hospital settings; this trend appears to be lasting over time. Similarly, the weekly all-cause mortality registered a significant reduction after the start of the vaccination campaign, and it remained stationary from February 2021 onwards.

Moreover, hospital burden and mortality were lower, and this finding could be explained by the effect of the partial immunization of the at-risk population. These figures reflect the implementation of health policy measures defined by the Italian national and regional governments during the second and third waves, as well as the rapid development and rollout of COVID-19 vaccines and the great effort of the national government to organize the vaccination campaign.

Vaccination campaign: strategies and policies

At the beginning of December 2020, a strategic immunization plan containing recommendations for first-priority groups (front-line healthcare workers and elderly people) was timely issued by the Ministry of Health [34], and at the end of the month (Table 1) Italy started the largest vaccination campaign in its history [35]. As a member state of the European Union (EU), Italy relied on the European Commission for vaccine supply. Specifically, the European Commission offered to run a single central procurement procedure on behalf of all member states, with a view to signing EU level Advance Purchase Agreements (APAs) with vaccine manufacturers. Those APAs included up-front EU financing to de-risk essential investments in order to increase the speed and scale of manufacturing successful vaccines. In return, the APAs provided the right – or under specific circumstances the obligation – to participating member states to buy a specific number of vaccine doses within a given timeframe and at a given price [cita]. The Italian vaccination campaign was coordinated by a national committee (composed by the Ministry of Health, Extraordinary Commissioner for the Emergency, National Institute of Health, and other national agencies), but the management and planning of vaccines administration were assigned to regional and provincial governments. Indeed, the Italian healthcare system is a national health service that guarantees a universal health coverage to all residents, ensuring that the general objectives and fundamental principles are met, but the responsibility of the delivery of essential levels of assistance to the population is delegated to the regions [36]; thus, the regional healthcare systems could make autonomous decisions regarding the vaccination campaign rollout. During this phase, some regions adopted a more centralized approach with a higher number of vaccination centers set up in hospitals. Campania and Lombardy, the

two most populous regions of Italy, adopted this approach and had fewer than 3 vaccination sites per 100,000 population (Fig. 5). Other regions adopted a different, decentralized approach, relying more on territorial public health agencies (Fig. 5). For example, Puglia and Liguria relied on existing Local Health Authorities (Aziende Sanitarie Locali) for vaccination administration, so there were between 10 and 20 vaccination centers per 100,000 population. These approaches are linked to the different territorial and socio-demographic features of each region and reflect the organization of the existing regional healthcare system [37]. Despite these stark differences in governance and management, the outcome of the vaccination campaign at the regional levels were similar. Indeed, the growing vaccine coverage rate for each age group had a similar pattern in the 21 regions and autonomous provinces investigated, as shown in Figs. 2-4 and S1-2.

The COVID-19 vaccination campaign was the largest and fastest vaccination campaign in Italian history, and came with its own set of challenges, some of which linked to vaccine availability and population eligibility. Vaccine rollout and administration was tied to the provisions supplied by the EU and the pharmaceutical companies, leading to a different articulation of the campaign throughout the pandemic, with different vaccines administered at different times (Figure S3). From January to March 2021 (Fig S2, Fig. S3), the limited availability of vaccines allowed the immunization of high-risk subpopulations as defined by Italy's Technical-Scientific Committee: healthcare and law enforcement personnel, together with elderly (≥ 80 years) and fragile people.

The second phase of the vaccination campaign started in March 2021 (Fig. 2-4). The vaccination was made available for people aged ≥ 18 years, but the priority was given to the older population with the enrollment of subsequent age classes. In this phase, the vaccination was

also offered to other working categories such as teachers and schools' personnel independently from age [34]. The declared goal of the campaign was to immunize at least 80% of the >12 -year-old population by the end of September 2021. By October 10, 2021, the number of fully vaccinated individuals in Italy was 43,229,551 (76.9% of the eligible population).

Given the global shortage of vaccines at the beginning of the campaign, the Italian COVID-19 Strategic Plan did not include migrants and minorities as priority groups [34]. Furthermore, the digital registration system was only accessible through a social security number, which limited vaccine accessibility to Italian residents. Starting from the summer of 2021, regional and local authorities activated specific access points for target at-risk subpopulations [38]. This was mainly due to the need for equitable and uniform vaccine coverage throughout the Italian territory and to reduce the risk of high viral circulation within specific population subgroups.

As shown in Figure S2, the weekly number of doses administered increased steadily until August 2021 and then started to decrease. In June 2021, the vaccination campaign reached the rate of more than 4 million doses administered per week (Fig S2), reaching a peak of 550,269 daily doses administered by June 4, 2021. Simultaneously, the incidence of COVID-19 decreased (Fig 1), leading the Italian government to suspend some control measures such as the required use of face masks outdoors. Reasons for this slowdown in the vaccination campaign can be found in a saturation of the easily accessible portion of the population. The remaining portion was represented by hard-to-reach individuals, including those hesitant about and opposed to vaccination.

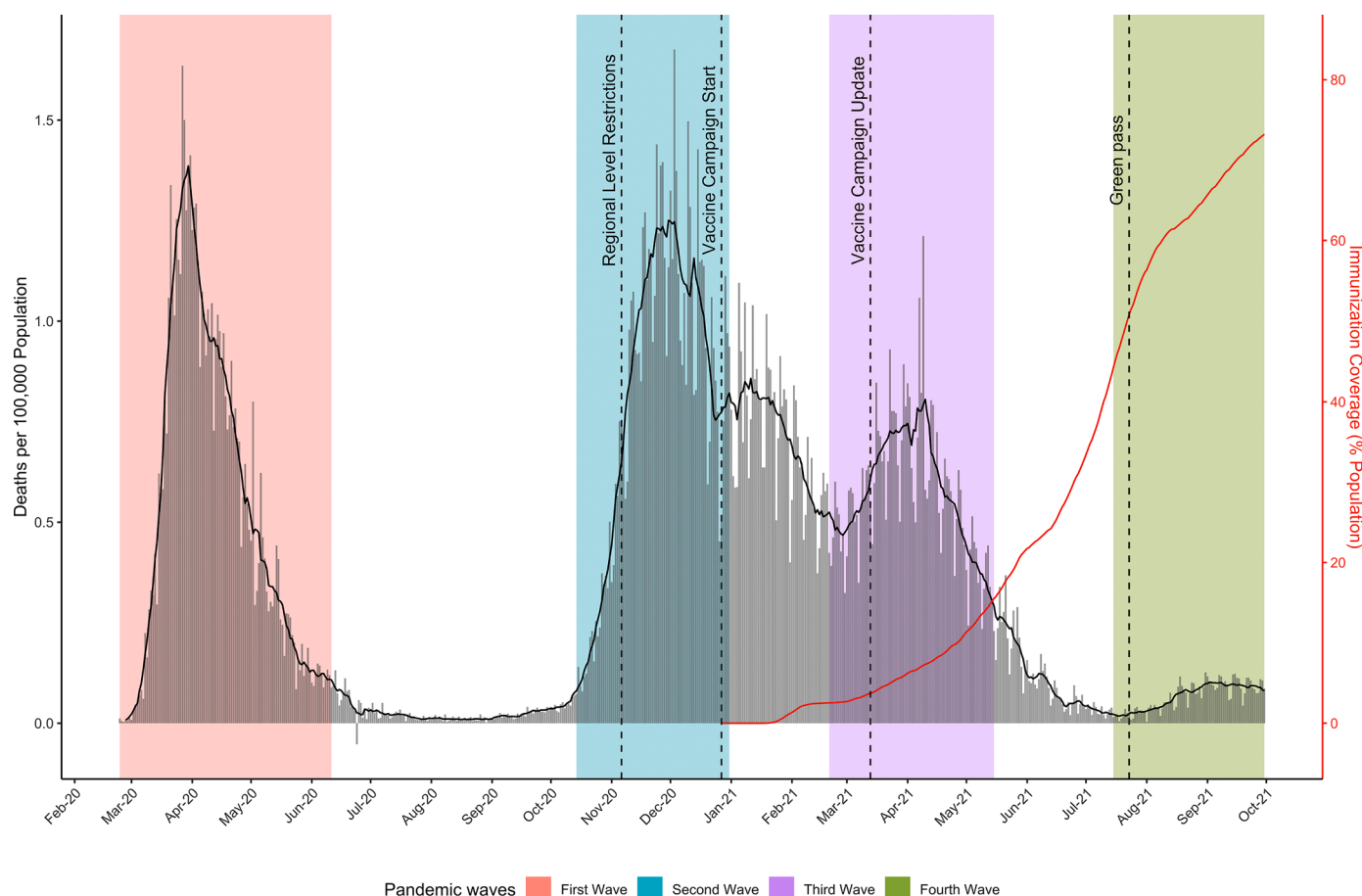


Fig. 4. Health policy measures, population immunization coverage, and COVID-19-related deaths in Italy (per 100,000 population).

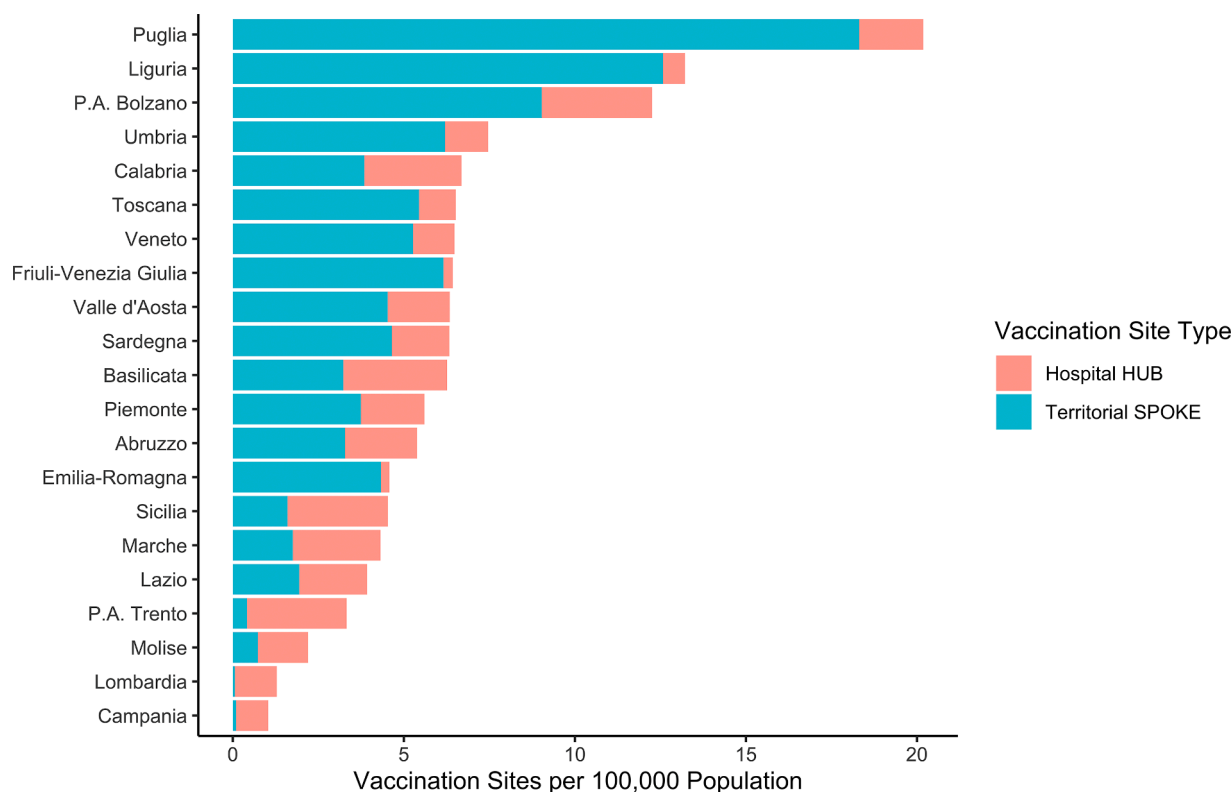


Fig. 5. Vaccination centers per 100,000 population, by region.

Fourth wave: the impact of vaccine rollout strategy

During the fourth wave of the pandemic (mid-July 2021 – October 2021), new cases, deaths, and hospitalizations were dramatically lower as compared to the previous waves (Fig. 2-4). The CFR (Fig. 1), which was similarly high during the second and third wave - albeit lower than that of the first wave - was much lower during the fourth one. As stated earlier, vaccines are the most effective technology to contain the COVID-19 pandemic and can be considered as the cornerstone that profoundly changed the dynamic of the pandemic in Italy. Thanks to the immune protection of the most fragile segments of the population, the fourth wave of the pandemic had a less heavy impact in terms of both healthcare utilization and deaths.

However, unlike other countries such as the United Kingdom, together with the vaccination several containment measures continued to be in place in Italy to counteract SARS-CoV-2 transmission. The good results obtained underline the importance of combined strategies. Maintaining the non-pharmaceutical interventions such as social distancing and the use of face masks indoors and introducing a mandatory Green Pass to nudge the population to get vaccinated, made it possible to keep a low viral transmission even in the early stages of the vaccination campaign, when vaccine coverage was largely incomplete. The data reported here show that after the first disrupting impact of the pandemic, especially in Northern Italy, the containment policies and the tier system of the regions put in place contributed to control the first and the subsequent waves until a vaccine was available. The vaccination strategy adopted as well as policies targeted to making available the vaccine (active offer of the vaccination, vaccination hubs) together with a nudging strategy (Green Pass) had a great impact on the diffusion of the infection and on the number of hospitalizations and deaths. However, it is important to highlight that this success story is marked not only by the vaccination campaign, but also by the maintenance of non-pharmaceutical interventions [39], such as requiring social distancing and the use of face masks indoors.

Conclusions

In this study, we described the evolution of the pandemic in Italy from March 2020 to October 2021. The data reported here further reinforce the evidence on the mutability of the pandemic and on the dramatic role of the vaccination campaign in reducing the impact of SARS-CoV-2 infection on the population, as well as non-pharmaceutical interventions.

The system was taken by surprise by the first wave that hardly hit the country, especially in Northern Italy, leading to an unprecedented health crisis and death toll. The lack of personal protective equipment, diagnostic capacities and capabilities, effective treatments and technologies to support the fight against the new pathogen led to the need for extreme policy, i.e. a national lockdown. The second wave in autumn 2020 was characterized by improved diagnostic capacity and better clinical management, leading to a decreased CFR. In this phase, the tier system was successfully implemented without a full total lockdown. However, the major difference observed during the third and fourth waves of the pandemic was made by the COVID-19 vaccination introduction and subsequent strategies and policies adopted for the implementation of the vaccination campaign.

Finally, the analysis illustrates the importance of multifaceted interventions. In particular, non-pharmaceutical interventions such as mandatory social distancing and use of facial masks, strongly contributed to the control of the pandemic before a vaccine was widely available. Subsequently, maintaining these policies helped encourage compliance with immunization.

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Declaration of Competing Interests

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:[10.1016/j.hlpt.2022.100604](https://doi.org/10.1016/j.hlpt.2022.100604).

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