



COVID-19

Evolution of SARS-CoV-2 epidemics in pediatric population in Liguria (North-west Italy) from March 2020 to December 2022: what could we have learned?

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Keywords

SARS-CoV-2 • Pediatric population • Liguria

Summary

Introduction. This retrospective analysis aims to follow the course of SARS-CoV-2 infections in pediatric population residing in Liguria, North-west Italy, from March 2020 to December 2022 and to relate it to the regional and national containment measures adopted, to assess the representativeness of the infection rate observed at the national level and to analyze the vaccination rates in different pediatric groups.

Methods. First episodes of SARS-CoV-2 infections registered in the national surveillance system were extracted and further anonymously analyzed for subjects aging ≤ 19 years. The absolute number of cases diagnosed daily during each year was compared to the number of residents in the region and graphical representations were used to visualize the trends in infection rates both annually and weekly in each year. Through narrative analysis, the relationship between changes in IR and key social events was analyzed.

Applying the direct standardization method, the epidemiology of SARS-CoV-2 infection in pediatric population was compared with that observed in the same age group in Italy.

All analyses were performed using Stata and Microsoft Excel.

Results. In the study period, 106,537 (17.4%) cases of SARS-CoV-2 infection were registered in subjects ≤ 19 years, out of a total of 610,404 cases reported in Liguria during that period. In the summer of 2020 the IR was close to zero, while later we observed increases and decreases in the IR in relation to activities and social restrictions adopted. Direct standardization showed an almost perfect coincidence between the expected cases in Italy, based on the Liguria incidence, and the observed cases.

Conclusions. Our results show that, in absence of effective therapies and vaccines, strict non-medical interventions (e.g. use of masks, improving indoor ventilation, physical social distancing, general lockdown) can be the only actions to counter the spread of a respiratory infection.

Introduction

SARS-CoV-2 is the etiological agent of the COVID-19 pandemic that began in China at the end of 2019 and subsequently spread around the world, affecting both children and adults. In Italy, as in all other parts of the world, the incidence of severe illness in the pediatric population was significantly lower compared to adults, with most pediatric patients exhibiting mild symptoms or even being asymptomatic [1]. Nonetheless, certain severe conditions, such as Multisystem Inflammatory Syndrome in Children (MIS-C), although rare, were observed with an epidemiology that followed that of the infection [2, 3].

The primary objective of this retrospective analysis was to follow the course of SARS-CoV-2 infections in individuals aged ≤ 19 years (pediatric population) residing in Liguria, Northwest Italy, from March 2020 to December 2022 and in relation to the regional and national containment measures adopted. Secondary, it aimed to assess the representativeness of infection rate observed in pediatric patients residing in Liguria at the

national level and to analyze the vaccination rates in different pediatric groups. Regarding vaccinations, it should be noted that the vaccines were made available at the end of 2020 for people older than 18 years and in the first phase were administered to healthcare workers and fragile patients, while they were approved in June 2021 for the 11-17 age group and only in December for children aged 5-11. The vaccines have not been administered to children under the age of 5.

Materials and methods

First diagnosed episodes of SARS-CoV-2 infection registered in the national surveillance system [4] in Liguria, north-west Italy, from March 2020 to December 2022 were extracted and then further anonymously analyzed for subjects aging ≤ 19 years (pediatric population). This age cut-off was chosen to ensure that the entire school population was included up to the end of high school. In the first period, molecular tests based on RT-PCR (real-time polymerase chain reaction) were

Tab. I. Data and infection rate per 100,000 pediatric residents in Liguria by year.

Year	2020 (10 months)	2021	2022
Pediatric population, n	231,068	230,580	227,509
SARS-CoV-2 infections in pediatrics, n	6,867	18,957	80,713
Percentages of pediatric people with a first documented SARS-CoV-2 Infection, (95%CI)	2.97 (2.90-3.04)	8.22 (8.11-8.33)	35.48 (35.28-35.67)
Infection rate per 100,000 pediatric residents	2,971.85	8,221.44	35,476.84

mainly used to diagnose infection then, when antigenic tests became available and were equated with molecular tests, both were considered for diagnosis.

The absolute number of cases diagnosed daily during each year (March-December 2020, 2021, 2022) was compared to the number of residents in the region on January 1st of each year [5]. Graphical representations were used to visualize the trends in infection rates (infections per 100,000 residents, IR) both annually and weekly in each year. Through narrative analysis, we examined how changes in IR were related with key social events, such as containment measures and their modifications ordered by regional or national authorities, public activities such as crowds for recreational events and the opening or closing of schools.

The epidemiology of SARS-CoV-2 infection in pediatric population in Liguria was compared with that observed in the same age group in Italy [6], applying the direct standardization method.

Data on vaccinations were extracted [7] and the percentages of people who received a complete primary vaccination course according to vaccine type and age [8, 9] were calculated considering the age distribution of population in Liguria on January 1st, 2021 and 2022. All analyses were performed using Stata [10] and Microsoft Excel.

Results

Between March 2020 and December 2022, 106,537 (17.4%) cases of SARS-CoV-2 infection were registered in population aged ≤ 19 years, out of a total of 610,404 cases reported in Liguria during that period. Table I reports the overall annual IR while Figure 1 describes the distribution of weekly IRs from March 2020 to December 2022, for the pediatric age in Liguria.

Distribution of residents and infections are further detailed in Tables SI and SII.

The percentage of population with a first documented SARS-CoV-2 Infection over the 3 years increased markedly starting from about 3% in 2020 and exceeding 35% in 2022 with an average of 15.6%, 95% CI (11.5-20.8). It should be noted that these data are underestimated because unreported/ undiagnosed cases were not included.

In the following analysis the IR is depicted yearly. The Figures 2, 3 and 4 are not directly comparable because different scales were utilized for each graph, for a clearer description of IR trends.

The year 2020. The IR trend is graphically depicted in Figure 2.

From March to May. On March 8th, the Italian government declared a nationwide lockdown, which included the closure of schools and an almost complete stop of public

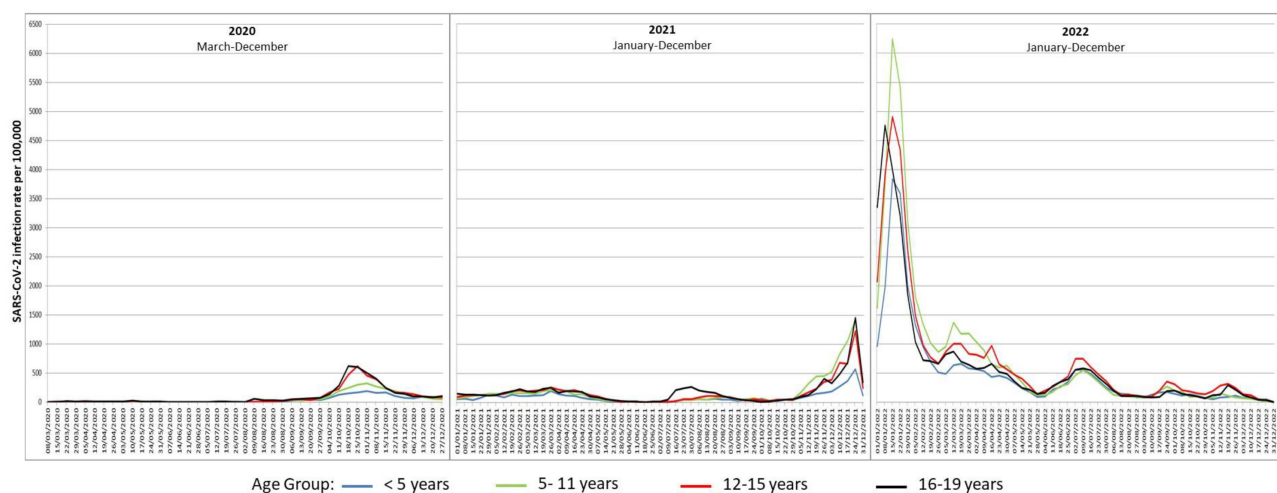
Fig. 1. Weekly rates of SARS-CoV-2 infection in pediatric population residing in Liguria by age group, in the period 2020-2022.

Fig. 2. Weekly rates of SARS-CoV-2 infection in pediatric population residing in Liguria by age group in 2020 (from March to December).

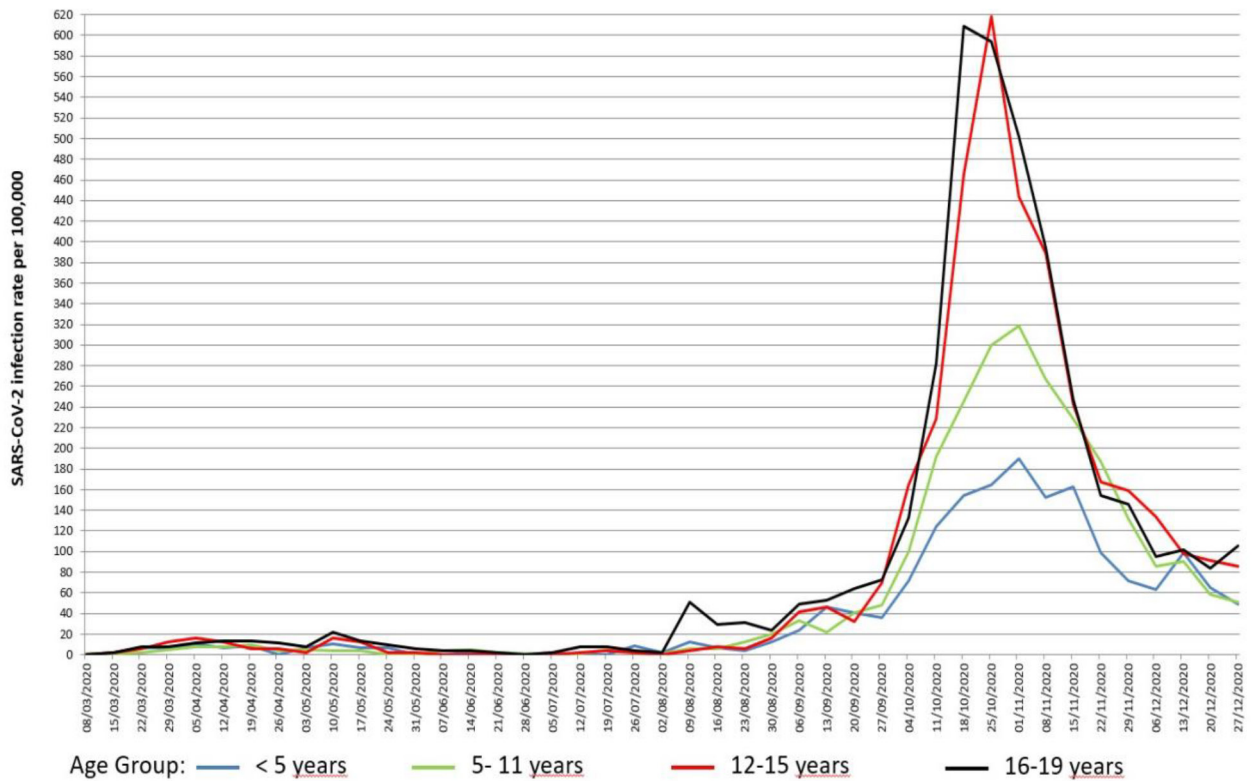


Fig. 3. Weekly rates of SARS-CoV-2 infection in pediatric population residing in Liguria by age group in 2021.

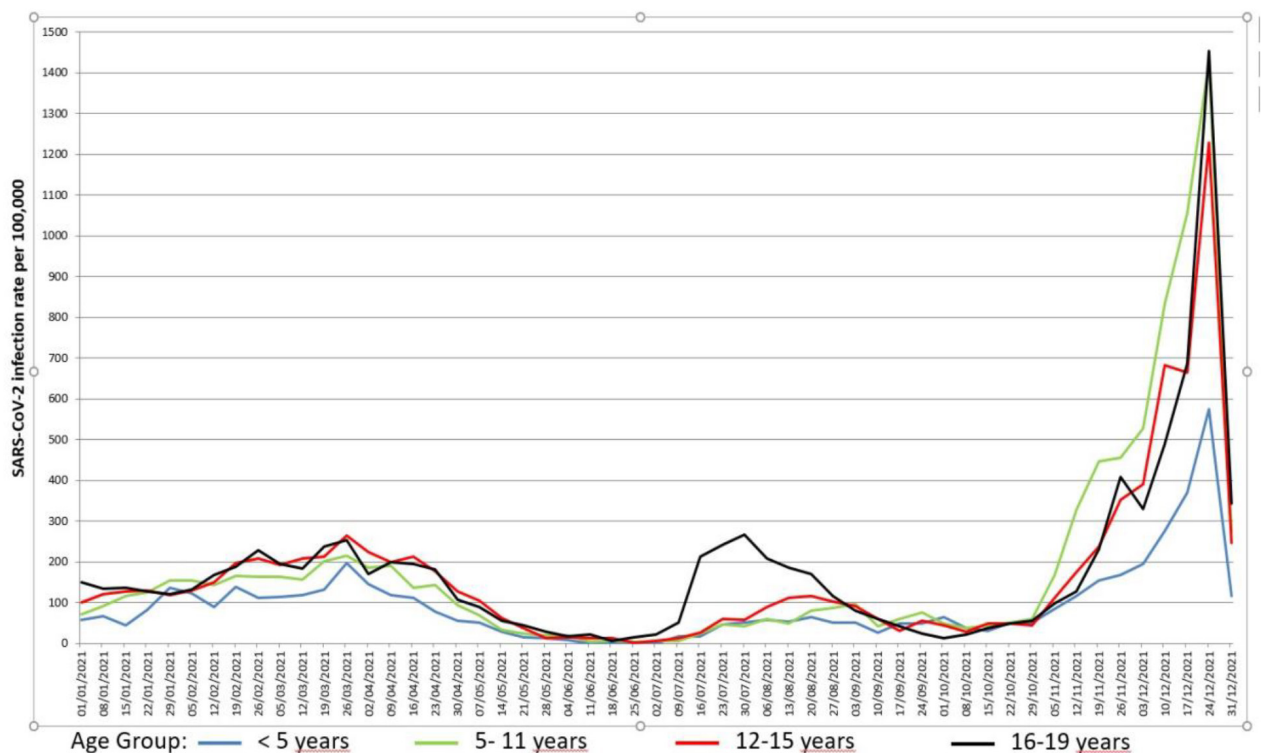
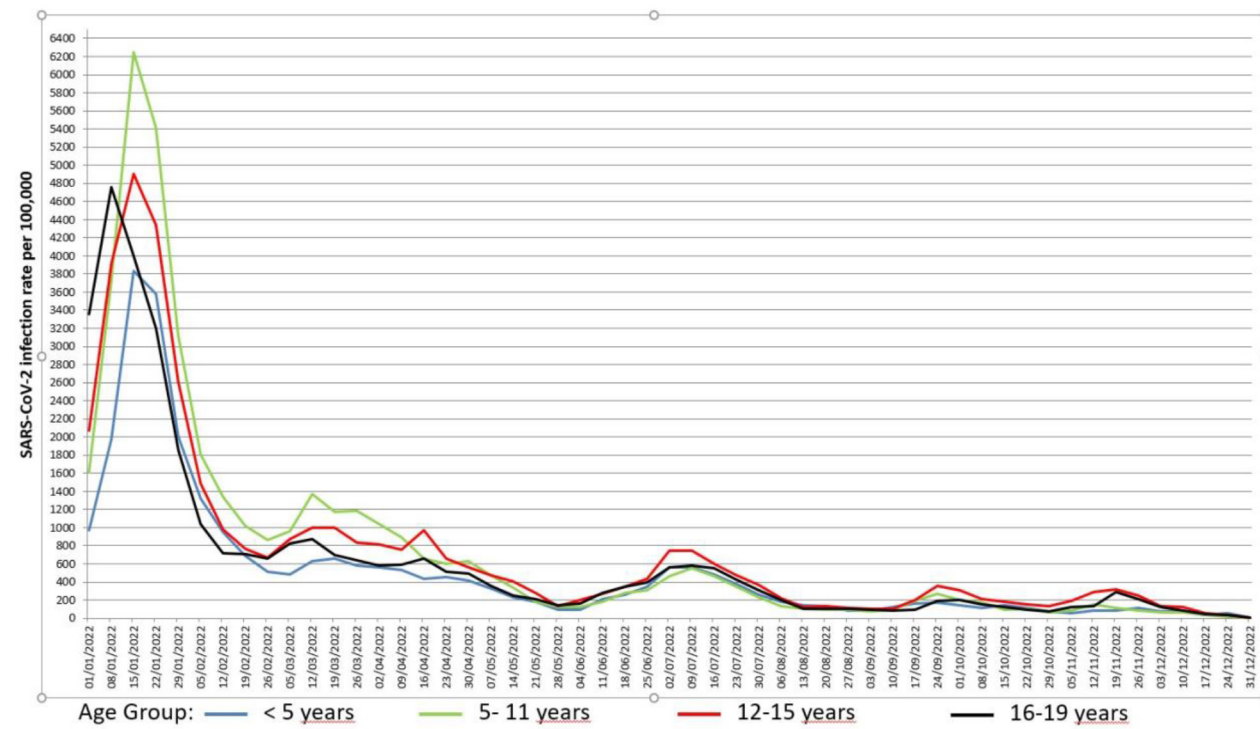
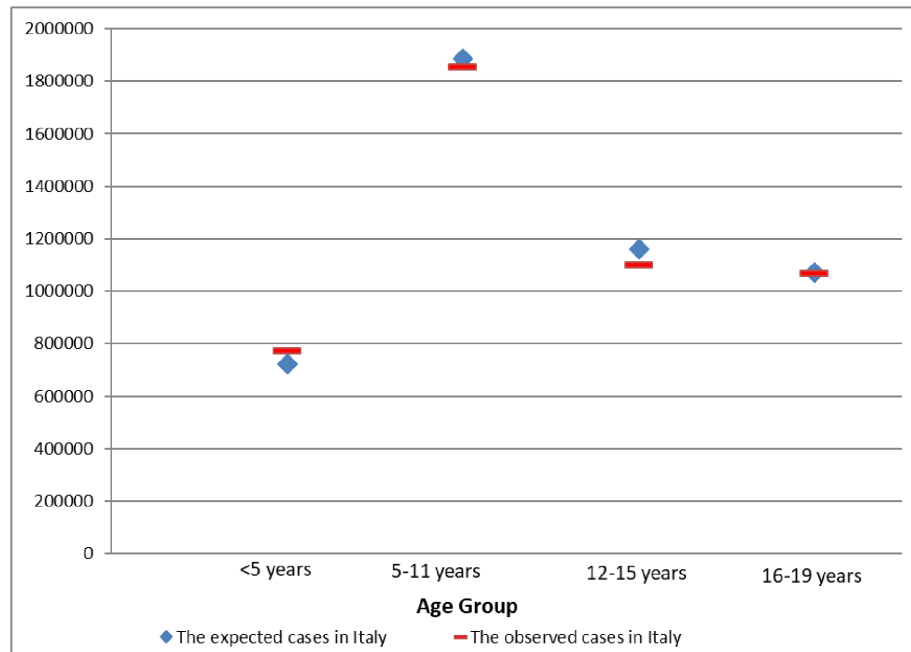


Fig. 4. Weekly rates of SARS-CoV-2 infection in pediatric population residing in Liguria by age group in 2022.**Fig. 5.** Comparison of expected and observed SARS-CoV-2 infection cases in the Italian pediatric population according to the observed incidence in Liguria.

transportation, with no movement possible except for exceptional reasons. This first phase of the pandemic was characterized by an extremely limited availability of diagnostic tests, initially reserved for adults with severe clinical illness. Even when diagnostic tests became available in sufficient quantities, the number of children

tested was small, mainly because of the very low clinical impact of the virus on the pediatric population. It is therefore plausible that the IR was largely underestimated during the first weeks of the pandemic. This consideration was true at least until May, when the availability of diagnostic tests improved significantly.

However, during these periods, the diagnosis of SARS-CoV-2 infection was still based only on molecular testing which likely underestimated the spread of the virus due to the difficulty in accessing testing.

From June to July. During this period the IR in the total and pediatric population showed values close to zero, with the consequent feeling in the public opinion that the epidemic at that time was now “behind us”: the restrictions had been eased, with a gradual return to “normal” life. The ban on public gatherings, social distancing and the requirement to wear a mask indoors remained in force, while public transport could operate at 50% of its capacity. Noteworthy, even if the IR remained low throughout the summer of 2020, some epidemic clusters occurred in various parts of the nation, especially where prevention measures were not respected. For example, around mid-August holidays in Sardinia there was an epidemic cluster linked to gatherings of people without protective devices during events/parties in well-known nightclubs-discos.

From August to December. An increase of IR (60.3) was observed in 16-19 years old residents in Liguria from August 2nd, while the rate in other pediatric ages remained constantly low. From end of August 2020 the IR increased also in other age groups. This phenomenon could be related initially with an increase of the public transport capacity from 50% to 80% followed by the start of the new school year. From September 14th in-person teaching was activated for all classes in Liguria and the IR constantly increased in all ages group with a modest slowdown after 20th-21st September when regional elections were held, with polling stations opened in schools with consequent interruption of in-person teaching. The reopening of schools meant that thousands of students began attending school again, socialize in the school environment, but mainly outside school and on public transport. This was especially true for those in high school (12-19 years) even if an increase of IR could be observed for all pediatric ages. Consequently, new restrictions were adopted such as mandatory use of protective masks in closed places other than private homes and in all outdoor places; closure of all activities where people could gather (restaurants, theatres, cinema halls, gyms, swimming pools) from 6.00 pm. Furthermore, in Liguria, 75% of high school lessons switched to distance learning while elementary and secondary schools teaching remained in person. Public transport capacity decreased to 60%. After these measures there was a slight reduction in the IR in adolescents (Fig. 2, black line) not considered sufficient and not observed in the general population (data not shown). As a consequence of general epidemiology, a ban on outdoor circulation from 10.00 pm to 5.00 am was established, with travel permitted in this time slot only for work needs or proven health and necessity reasons; distance learning involved also secondary school, and the capacity of public transport was further reduced to 50%. Then, the curve, from the first days of November, reversed its dynamics and dropped rapidly over seven weeks, with a small flex for the 16-19 age group in concomitance with the Christmas holidays.

The year 2021. The IR trend is graphically depicted in Figure 3.

From January to October. From January 2021, a positive case of infection could also be defined by means of an antigen detection test (with sensitivity of at least 80% and a specificity 97% compared with that of RT-PCR), which, due to their simplicity and speed of execution, allowed better definition and control of the spread of the virus. Important limitations on travel and social life activities were introduced sporadically [mainly on New Year's Eve, January 1st and Easter (April 4th)]. Moreover, at the end of 2020 a nationwide vaccination program was implemented, starting with healthcare workers, followed by the general population in 2021. Noteworthy, in the second half of June (11th) the final phase of the European Football Championship began and the good performance of the Italian team led people (including many adolescents) to gather to watch the matches on large screens in the squares, in public places and in private homes, for quite long periods of time (2-3 hours for at least the last 3 matches) and to shout and hug in correlation with victories. This period was followed by an increase of the IR especially in the 12-19 years group. Then, the incidence continued to increase during the Olympic Games (weeks #29-31), although at a slower rate, since probably a smaller audience (and for shorter periods of time) crowded, despite the victories of Italian athletes in important competitions. In the following weeks the IR slowed down until the end of October.

From November to December. Starting in November, the IR began to rise again, with a dynamic completely different from that observed in the previous periods, reaching its highest peak of 2021 in all age groups, but especially in school-aged subjects, leading to further restrictions (requirement to wear masks in closed places). In this period the SARS-CoV-2 Delta variant was predominant, while the Omicron variant began to spread.

The year 2022. The IR trend is graphically depicted in Figure 4.

From January to December. From the beginning of 2022 the Omicron variant became predominant in Italy, but after the peak in January (IR > 6200) the IR decreased and restrictions were gradually removed.

How representative can these results be of Italian epidemiology in pediatrics? As shown in Figure 5, direct standardization shows an almost perfect coincidence between the expected cases in Italy, based on the Liguria incidence, and the observed cases.

The rates of vaccination. Starting from the last weeks of 2020, an anti SARS-Cov-2 vaccination campaign began in Italy, but pediatric patients were involved later and in different times (Tab. II).

Noteworthy, 68.1% of people aging 12-19 years received a complete cycle of vaccinations in 2021 versus 10.5% in 2022. This trend was more evident among adults, where the percentage was 82.8% in 2021 and only 4.1% in 2022.

Tab. II. Distribution of people who received a complete 1st vaccination course in Liguria by age group.

Age group	Number of vaccinations/population (%)	
	2021	2022
< 5 y	0/46,991	0/45,678
5-11 y	0/80,932	20,843/78,863 (26.4)
12-19 y	69,943/102,657 (68.1)	10,858/102,968 (10.5)
20-90+ y	1,066,108/1,287,915 (82.8)	52,125/1,281,718 (4.1)

Years: y.

Figure 6 shows the SARS-CoV-2 infections and vaccinations rates per 100,000 residents in relation to the progress of the vaccination campaign for the different age groups. The highest rates of vaccinations were observed in 2 peaks at the beginning of the campaign for 12-19 years of age in 2021 and during the summer season, followed by a lower, third peak at the end of this year. At the beginning of the vaccination campaign for the youngest (5-11 years old), in the first four months of 2022, there was higher peak for this age group compared to both the adolescent/young (12-19 years old) and adult population.

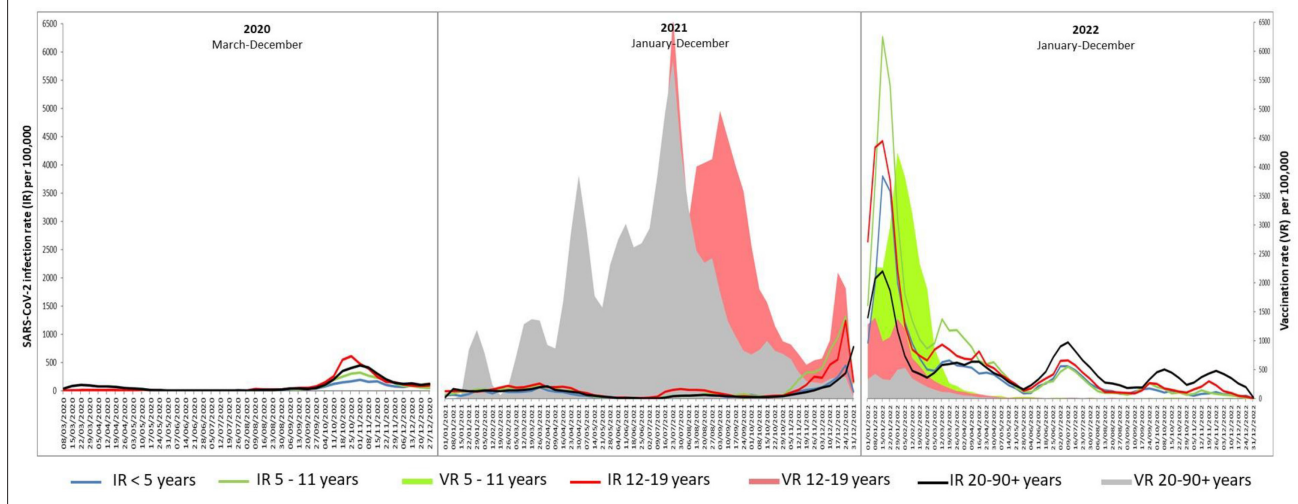
Discussion

This retrospective study provides an overview of the first three years of the SARS-CoV-2 pandemic among pediatric residents in Liguria, northwestern Italy, and shows that approximately half of the pediatric population residing in this region had at least one documented SARS-CoV-2 infection by December 2022. Considering asymptomatic subjects or others not notified, it is likely that the prevalence of the infection is higher than reported in Italy and Western Europe in the same observation period [11]. Despite the relatively small population size in Liguria (resident population in

January 2022 $n = 1,509,277$, population aged 0-19 years $n = 227,509$ (15.1%)), our results suggest that the trends observed in Liguria are representative of those across Italy in this population. Therefore, our results can be extrapolated to the broader Italian pediatric population and provide insight into management strategies for potential future pandemic respiratory infections in young people [12]. However, it is important to recognize a bias in the assessment of IR in the pediatric population during the early months of the pandemic due to the limited availability of diagnostic tests, which were primarily reserved for severe or symptomatic cases. As children and adolescents were often asymptomatic or had mild symptoms, this limitation may have contributed to an even greater underestimation of cases among them. Conversely, the reliability of IR data has increased with the improvement in testing capacity, particularly since mid-2020.

Our analysis shows a clear association between the incidence of SARS-CoV-2 in pediatric patients, especially adolescents, and specific gatherings and activities, such as sports events attended by large crowds and victory celebrations. This association underscores the role of certain events in facilitating the spread of the virus, as already highlighted [13]. Increased crowding on public transportation and the reopening of schools were also associated with rising IRs, suggesting that these settings played a significant role in the dynamics of transmission among adolescents [14, 15]. While transmission in pediatrics is likely to have occurred primarily within the family environment [16], schools have emerged as key sites for virus spread, as suggested by the observation of a higher incidence among school staff than in the general population, and particularly during periods of face-to-face teaching [14, 17]. The role of “social activities” is further confirmed by the increase of IR when the extra-scholastic containment measures were “relaxed” (December 2021-January 2022) [18, 20]. This period coincided in Italy with the replacement of the Delta

Fig. 6. Progress of the vaccination campaign (vaccination rate, VR) and infection rate (IR) of SARS-CoV-2 in the Ligurian population by age group.



variant by Omicron [21], which had a similar incubation period but a shorter generation interval [22, 23], further increasing the spread of the virus also in pediatrics. All these observations underline that, in absence of effective therapies and vaccines, only strict non-medical interventions such as promoting the use of masks, improving indoor ventilation, and advocating physical social distancing, up to general lockdown as an extreme measure, can be the only actions to counter the spread of a severe respiratory infection [18, 20]. However, these measures have come at a significant cost to human well-being, particularly in the pediatric population and especially in adolescents [24]. These aspects, with their pros and cons for the health of society, should be kept in mind in the future to identify the most appropriate control measures in the event of a new respiratory virus pandemic [12].

Final considerations must be made for vaccination programs, which represent a pivotal strategy for controlling infections. In Italy, vaccination against SARS-CoV-2 for young people started at the end of 2021 for those aged ≥ 18 years, but became available in June for those aged 12 to 18 years and only in December 2021 for children aged 5 to 11 years. There were differences in vaccination rates between the two groups of vaccine-eligible pediatrics, as observed in other series [26, 27], with subjects aged 12-19 years having higher rates, likely due to factors such as accessibility, peer influence, personal autonomy, and high educational background and family vaccination rates [27, 28]. In contrast, vaccination rates among children aged 5-11 years remained lower, as previously reported [29, 30], likely influenced by parental decisions shaped by concerns about safety, efficacy, and misinformation. Vaccination programs represent a central strategy for controlling infectious diseases, but the complexity of decision making, influenced by individual motivations, peer influence, and parental concerns, underscores the need for targeted public health initiatives to improve vaccine uptake in all age groups.

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Conflict of interest statement

The authors declare no conflict of interest.

Authors' contributions

MM, FB, RS, EC, CS, GI: conceptualization and methodology; MM, FB: data collection, analysis and interpretation; writing-original draft preparation: MM, FB, RS, EC, CS; writing-review and editing: MM, FB,

RS, EC, CS, GI, IG; supervision MM, FB, RS, EC. MM and FB contributed equally to data collection, analysis and interpretation. All authors have agreed to the published version of the manuscript.

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