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Who Still Pays the Price of SARS-CoV-2 in the Vaccination Era? Evidence from Primary Healthcare in Greece

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Abstract

Background: Understanding how demographic and clinical factors influence SARS-CoV-2 infection patterns, vaccination uptake and disease outcomes in community settings is essential for effective primary care-based public health planning. Objectives: This study aimed to investigate the distribution of SARS-CoV-2 infections among adults attending Primary Healthcare (PHC) facilities in Giannitsa, Greece, from 2020 to 2024, and to examine associations between demographic and clinical characteristics, vaccination category and disease outcomes. Methods: A retrospective analysis was conducted using data from the National Registry of Patients with COVID-19. The study included 1144 adults diagnosed with SARS-CoV-2 at PHC facilities from 19 November 2020 to 3 October 2024; all cases included in the present analysis had been confirmed by rapid antigen testing. Variables included age, gender, residence, registry-recorded underlying medical conditions, vaccination category, seasonality and clinical outcome. Results: Significant shifts in case distribution were observed across time, with younger adults predominating in 2020–2022 and older adults (61–90 years) in 2023–2024 ($p < 0.001$). Winter months showed higher case incidence overall ($p < 0.001$). Vaccination coverage increased annually, reaching 84.8% in 2024 ($p < 0.001$). Hospitalization/death occurred in 1.7% of patients and was strongly associated with age ≥61 years (6.0% vs. 0.3%), the presence of at least one registry-recorded underlying medical condition (9.2% vs. 0.9%) and vaccination category; specifically, hospitalization/death occurred in 10.4% of individuals diagnosed during the pre-vaccine period, 2.3% of unvaccinated individuals during the vaccination era and 0.9% of vaccinated individuals (all $p < 0.001$). Conclusions: Older age, underlying medical conditions and a lack of vaccination were key predictors of worse outcomes. The findings underscore the importance of strengthening vaccination outreach and targeted PHC interventions, particularly for high-risk and rural populations.

Keywords: primary healthcare; SARS-CoV-2; vaccination status; epidemiological surveillance

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1. Introduction

The health crisis of 2020 was an unprecedented challenge that not only affected health systems and the economy, but also spread and had a deep social impact from many aspects [1]. As the patient's first point of contact with the healthcare system, Primary

Healthcare (PHC) should have had a central role in the management of the crisis. However, in the case of Greece and in spite of repeated legislative interventions, PHC is still poorly organized, with its services mainly focused on the management of acute cases, while its involvement in health promotion and disease prevention initiatives remains limited [2]. In addition, issues such as chronic understaffing and underfunding in terms of infrastructure and equipment have contributed to the persistence of a network of services that struggle to meet the needs of the population [3]. The health crisis thus served as a mirror that reflected the pathologies of the PHC system and increased the pressure for restructuring and implementing appropriate and innovative interventions in public health [4].

Understanding the epidemiological characteristics of a disease can become a critical weapon with a crucial contribution to the implementation of targeted interventions [5]. The ability to predict the risk of developing severe disease among patients infected with SARS-CoV-2 facilitates decision making by both healthcare providers and individuals. At the patient level, it informs evidence-based decision making regarding preventive strategies against the virus while at the healthcare provider level, the integration of risk factors with epidemiological models allows for accurate service planning and guides evidence-based resource allocation [6]. Since the early stages of the pandemic, a large number of studies—mainly from China—have addressed this topic, with the majority concerning hospitalized patients rather than patients in the community [7–9].

The intention to receive COVID-19 vaccination, along with the factors shaping it, has similarly attracted substantial research attention. Vaccination coverage showed significant differences among various countries, social groups, and age categories [10]. Factors such as gender, age, comorbidities and socioeconomic inequalities have been linked not only to the likelihood of receiving vaccination but also to the outcome of the disease [11,12]. The majority of the studies that discussed the factors affecting the intention to be vaccinated are based on questionnaires that are aimed at identifying attitudes and behaviors. Although these studies highlight important psychosocial determinants of vaccination behavior, they are limited by the subjectivity of the responses.

In Greece, so far, the available data on factors associated with disease outcome and vaccination status are limited, while globally the number of studies focusing on community-based patients and non-hospitalized patients is also restricted.

This study aimed to describe the distribution of SARS-CoV-2 infections among adults attending PHC settings in Giannitsa, Greece, and to examine associations between demographic and clinical characteristics, vaccination status and disease outcomes over the period 2020–2024.

2. Methods

2.1. Study Design and Setting

This retrospective observational study included 1144 adults diagnosed with SARS-CoV-2 infection at the three public Primary Healthcare (PHC) facilities of Giannitsa (Primary Healthcare Center, 13th Local Health Team, 17th Local Health Team [13]) from 19 November 2020 to 3 October 2024. All cases included in the present analysis were confirmed using a rapid antigen test performed at the COVID-19 Outpatient Clinic jointly operated by the three facilities, which share common premises. Eligible participants were adults aged 18 years or older with a registry-recorded SARS-CoV-2 diagnosis linked to this PHC testing pathway. Demographic and clinical data were retrieved from the National Registry of Patients with COVID-19, an integrated electronic platform linked to the national e-prescription system, the AMKA database, and the Electronic Personal Health Record. The study included adult patients ($\geq$18 years) with laboratory-confirmed SARS-CoV-2 infection who were registered during the study period. All data were anonymized and coded prior

to analysis. Given the retrospective and anonymized nature of the study, the requirement for written informed consent was waived by the approving authority. The study protocol was approved by the Scientific Council of Primary Healthcare of the 3rd Health Region of Macedonia (approval number: 10561/26-02-2025).

2.2. Data Sources and Study Population

Data were obtained from the National Registry of Patients with COVID-19, an integrated electronic platform linked to the national e-prescription system, the AMKA database and the Electronic Personal Health Record. Extracted variables included demographic characteristics (age, gender, residence), vaccination history, underlying medical conditions, month and year of diagnosis and final disease outcome. Residence was classified as urban or rural according to official administrative geographic designations. Underlying medical conditions included diabetes mellitus (type I or II) and immunosuppression and/or malignancy among patients receiving immunosuppressive or antineoplastic therapy at the time of diagnosis. The registry extract available for this study did not provide standardized information on several other established COVID-19 risk factors, including BMI/obesity, hypertension, broader cardiovascular disease, chronic respiratory disease, chronic kidney or liver disease, cerebrovascular disease, or previous SARS-CoV-2 infection history. Age was categorized into six groups (18–30, 31–40, 41–50, 51–60, 61–70 and 71–90 years). Each registry entry represented a diagnosis recorded during the study period; however, the available dataset did not allow us to reliably distinguish first infections from reinfections for the same individual. All data were anonymized prior to analysis.

2.3. Variables

Two dependent variables were examined: (1) disease outcome, categorized as recovery versus hospitalization and/or death, and (2) vaccination category, classified as pre-vaccine period, unvaccinated or fully vaccinated. The pre-vaccine period category refers to diagnoses recorded before vaccines became available and should not be interpreted as vaccine refusal or hesitancy. Fully vaccinated status followed national definitions requiring $\geq$21 days after completion of a two-dose or single-dose vaccination regimen. Independent variables included age, gender, place of residence, registry-recorded underlying medical conditions, season of diagnosis (winter or summer) and year of diagnosis. All variables were treated as categorical to accommodate the structure of the dataset and the retrospective nature of the analysis.

2.4. Statistical Analysis

Data management and coding were performed in Microsoft Excel 2016, and statistical analyses were conducted using IBM SPSS Statistics version 26 (IBM Corp., Armonk, NY, USA). Categorical variables were summarized as frequencies and percentages. Associations between variables were assessed using the chi-square test of independence. When Cochran's assumptions were not met—that is, when more than 20% of expected cell counts were below 5—Fisher's exact test was applied. A p-value < 0.05 was considered statistically significant.

3. Results

Among 1144 diagnosed patients, 42.4% were male and 57.6% were female. Nearly half of all cases occurred among individuals aged 41–60 years. Most patients resided in urban areas (71.9%). A total of 10.5% of patients had at least one underlying medical condition (7.2% diabetes; 3.3% immunosuppression or malignancy). Regarding vaccination, 61.0% of cases occurred among fully vaccinated individuals, 34.8% among unvaccinated

patients and 4.2% during the pre-vaccine period. Most patients recovered (98.3%), while 1.7% required hospitalization and/or died (Table 1).

Table 1. Epidemiological characteristics of the study population (N = 1144).

Parameter	Category	n (%)
Age group (years)	18–30	169 (14.8)
	31–40	159 (13.9)
	41–50	269 (23.5)
	51–60	264 (23.1)
	61–70	180 (15.7)
	71–90	103 (9.0)
Gender	Male	485 (42.4)
	Female	659 (57.6)
Place of residence	Urban	823 (71.9)
	Rural (settlements around urban area)	321 (28.1)
Underlying medical conditions	None	1024 (89.5)
	≥1 condition	120 (10.5)
Vaccination history	Pre-vaccine period	48 (4.2)
	Unvaccinated	398 (34.8)
	Fully vaccinated	698 (61.0)
Disease outcome	Recovery	1124 (98.3)
	Hospitalization and/or death	20 (1.7)

3.1. Temporal Trends in Case Distribution, Vaccination Status and Outcomes

Statistically significant differences in age distribution were observed across the different time periods ($\chi^2(15) = 57.212$, $p < 0.001$). Among individuals aged 18–30 years, the proportion of cases was higher in 2020–2021 (24.0%) and 2022 (16.4%) compared with 2023 (6.3%) and 2024 (3.8%), indicating a marked decrease over time. In contrast, cases in the 61–70 age group increased in 2023 (26.3%), while in the 71–90 age group a higher proportion of cases was observed in 2023 (12.0%) and 2024 (13.3%) compared with 2020–2021 (4.8%) and 2022 (8.6%). Overall, 46.6% of all cases during the study period occurred in individuals aged 41–60 years.

Seasonal analysis also revealed statistically significant differences ($\chi^2(3) = 71.051$, $p < 0.001$). Across the entire period (2020–2024), slightly more cases occurred in winter (54.5%) than in summer (45.5%). The proportion of cases occurring in winter was higher in 2020–2021 (66.5%) and 2023 (78.3%), whereas in 2022 a higher proportion of cases was observed during the summer months (54.2%).

Regarding vaccination status, statistically significant differences in case distribution across time periods were observed ($\chi^2(6) = 353.164$, $p < 0.001$). During the pre-vaccine period, cases accounted for 4.2% of the total sample. The proportion of vaccinated patients increased from 37.1% in 2020–2021 to 58.1% in 2022, 81.1% in 2023 and 84.8% in 2024.

Disease outcomes also differed significantly by time period ($\chi^2(1) = 20.464$, $p < 0.001$). Hospitalization/death was more frequent in 2020–2021 (6.0%) compared with 2022–2024 (1.0%). Overall, hospitalization or death occurred in 1.7% of cases during the entire study period (Table 2).

Table 2. Frequency of SARS-CoV-2 infections and key characteristics by year.

Variable	Category	Overall, n (%)	2020–2021, n (%)	2022, n (%)	2023, n (%)	2024, n (%)	Test Statistic	*p*-Value
Total cases		1144 (100)	167 (14.6)	697 (60.9)	175 (15.3)	105 (9.2)	$\chi^2(3) = 797.78$	<0.001
Gender	Male	485 (42.4)	76 (45.5)	296 (42.5)	71 (40.6)	42 (40.0)	$\chi^2(3) = 1.150$	0.765
	Female	659 (57.6)	91 (54.5)	401 (57.5)	104 (59.4)	63 (60.0)		
Age group (years)	18–30	169 (14.8)	—	—	—	—	$\chi^2(15) = 57.212$	<0.001
	31–40	159 (13.9)	—	—	—	—		
	41–50	269 (23.5)	—	—	—	—		
	51–60	264 (23.1)	—	—	—	—		
	61–70	180 (15.7)	—	—	—	—		
	71–90	103 (9.0)	—	—	—	—		
Place of residence	Urban	823 (71.9)	—	—	—	—	$\chi^2(3) = 4.130$	0.248
	Rural	321 (28.1)	—	—	—	—		
Season	Winter	623 (54.5)	111 (66.5)	319 (45.8)	137 (78.3)	56 (53.3)	$\chi^2(3) = 71.051$	<0.001
	Summer	521 (45.5)	56 (33.5)	378 (54.2)	38 (21.7)	49 (46.7)		
Vaccination category	Pre-vaccine †	48 (4.2)	48 (28.7)	0 (0.0)	0 (0.0)	0 (0.0)	$\chi^2(6) = 353.164$	<0.001
	Unvaccinated	398 (34.8)	57 (34.1)	292 (41.9)	33 (18.9)	16 (15.2)		
	Vaccinated	698 (61.0)	62 (37.1)	405 (58.1)	142 (81.1)	89 (84.8)		
Disease outcome ‡	Recovery	1124 (98.3)	157 (94.0)	—	—	—	Fisher's exact test = 20.464	<0.001
	Hospitalization/death	20 (1.7)	10 (6.0)	—	—	—		

† Pre-vaccine refers to diagnoses before vaccine availability and should not be interpreted as vaccine refusal or hesitancy. ‡ Outcome comparison was analyzed as 2020–2021 vs. 2022–2024 combined because of sparse severe events. For 2022–2024 combined, recovery/hospitalization–death was 967 (99.0%)/10 (1.0%).

3.2. Factors Associated with Disease Outcomes

Across the entire study period, disease outcome was significantly associated with age, a history of underlying medical conditions and vaccination status (Table 3).

Table 3. Association between disease outcome and independent variables.

Variable	Category	Recovery n (%)	Hospitalization/Death n (%)	Test Statistic	*p*-Value
Gender	Male	476 (98.1)	9 (1.9)	$\chi^2(1) = 0.057$	0.812
	Female	648 (98.3)	11 (1.7)		
Age	18–60 years	858 (99.7)	3 (0.3)	$\chi^2(1) = 39.705$ [a]	<0.001
	61–90 years	266 (94.0)	17 (6.0)		
Place of residence	Urban	811 (98.5)	12 (1.5)	$\chi^2(1) = 1.438$	0.231
Season	Winter	615 (98.7)	8 (1.3)	$\chi^2(1) = 1.716$	0.190
	Summer	509 (97.7)	12 (2.3)		
Underlying medical conditions	None	1015 (99.1)	9 (0.9)	$\chi^2(1) = 42.952$ [a]	<0.001
	≥1 condition	109 (90.8)	11 (9.2)		

Table 3. *Cont.*

Variable	Category	Recovery n (%)	Hospitalization/Death n (%)	Test Statistic	*p*-Value
Vaccination status	Pre-vaccine †	43 (89.6)	5 (10.4)	$\chi^2(2) = 24.817$ [a]	<0.001
	Unvaccinated	389 (97.7)	9 (2.3)		
	Vaccinated	692 (99.1)	6 (0.9)		

[a] Fisher's exact test applied where Cochran's assumptions were not met. † Pre-vaccine refers to diagnoses before vaccine availability and should not be interpreted as vaccine refusal or hesitancy.

Patients aged 61–90 years had a markedly higher rate of hospitalization/death (6.0%) compared with those aged 18–60 years (0.3%; $\chi^2(1) = 39.705$, $p < 0.001$). Similarly, patients with at least one underlying medical condition had a higher rate of hospitalization/death (9.2%) than those without such conditions (0.9%; $\chi^2(1) = 42.952$, $p < 0.001$).

Vaccination status was also strongly associated with outcome ($\chi^2(2) = 24.817$, $p < 0.001$). Hospitalization/death occurred in 10.4% of patients in the pre-vaccine period, 2.3% of unvaccinated patients during the vaccination era and only 0.9% of vaccinated patients. No statistically significant associations were identified between disease outcome and gender, place of residence or season.

3.3. Factors Associated with Vaccination Status

Vaccination status against SARS-CoV-2 was significantly associated with age ($\chi^2(10) = 44.522$, $p < 0.001$), place of residence ($\chi^2(2) = 8.324$, $p = 0.016$), season ($\chi^2(2) = 28.417$, $p < 0.001$) and history of underlying medical conditions ($\chi^2(2) = 22.720$, $p < 0.001$) (Table 4).

Table 4. Association between vaccination status and independent variables.

Variable	Category	Pre-Vaccine n (%)	Unvaccinated n (%)	Vaccinated n (%)	Test Statistic	*p*-Value
Gender	Male	22 (4.5)	165 (34.0)	298 (61.4)	$\chi^2(2) = 0.401$	0.818
	Female	26 (3.9)	233 (35.4)	400 (60.7)		
Age group (years)	18–30	8 (4.7)	78 (46.2)	83 (49.1)	$\chi^2(10) = 44.522$	<0.001
	31–40	6 (3.8)	68 (42.8)	85 (53.5)		
	41–50	11 (4.1)	111 (41.3)	147 (54.6)		
	51–60	13 (4.9)	78 (29.5)	173 (65.5)		
	61–70	6 (3.3)	42 (23.3)	132 (73.3)		
	71–90	4 (3.9)	21 (20.4)	78 (75.7)		
Place of residence	Urban	41 (5.0)	270 (32.8)	512 (62.2)	$\chi^2(2) = 8.324$	0.016
	Rural	7 (2.2)	128 (39.9)	186 (57.9)		
Season	Winter	18 (2.9)	182 (29.2)	423 (67.9)	$\chi^2(2) = 28.417$	<0.001
	Summer	30 (5.8)	216 (41.5)	275 (52.8)		
Underlying medical conditions	None	39 (3.8)	379 (37.0)	606 (59.2)	$\chi^2(2) = 22.720$	<0.001
	≥1 condition	9 (7.5)	19 (15.8)	92 (76.7)		

Vaccination coverage increased with age, ranging from 49.1% in the 18–30 age group to 75.7% in those aged 71–90 years. Higher vaccination rates were also observed among residents of urban areas compared with those living in rural settlements (62.2% vs. 57.9%), during the winter months compared with summer (67.9% vs. 52.8%) and among individuals with at least one underlying medical condition (76.7%) compared with those without such conditions (59.2%). No statistically significant association was found between vaccination status and gender.

4. Discussion

The analysis of case distribution across the study period showed significant variation by age, seasonality, vaccination status and disease outcome. During 2020–2022, younger adults aged 18–30 years accounted for a higher proportion of cases, while a clear shift toward older age groups was observed in 2023–2024. This pattern likely reflects differences in social activity and adherence to preventive measures among younger adults early in the pandemic, combined with changing epidemiological dynamics over time. The increasing burden among older individuals in 2023 may be associated with waning vaccine-induced immunity, the circulation of new viral variants or the cumulative effects of pandemic fatigue [14,15].

Seasonal variation was also evident, with significantly higher incidence during the winter months. This aligns with the well-documented seasonal behavior of respiratory viruses, facilitated by increased indoor crowding and the effects of temperature and humidity on viral survival. Low temperature and low humidity have been associated with greater transmissibility of coronaviruses such as SARS-CoV and MERS-CoV [16], and similar associations have been reported for SARS-CoV-2 [17]. A comparative study in Italy likewise showed higher COVID-19 case numbers, hospital admissions and ICU admissions during winter months, independent of vaccination coverage or non-pharmaceutical interventions [18].

Vaccination patterns showed substantial improvement after 2022, reflecting increased vaccine availability and growing public confidence. The markedly higher hospitalization and mortality rates during 2020–2021 compared with later years can be attributed to both rising vaccination coverage and advancements in clinical management and therapeutic protocols over time.

Disease outcome was consistently associated with age, underlying medical conditions and vaccination status. These findings corroborate international evidence identifying older adults and individuals with comorbidities as high-risk groups for severe disease and mortality [19–23]. However, the registry captured only a limited subset of clinically relevant comorbidities. Important established risk factors such as BMI/obesity, hypertension, broader cardiovascular disease, chronic respiratory disease, chronic kidney or liver disease, and cerebrovascular disease were not available in the extract used for this study. Therefore, the variable "underlying medical conditions" should be interpreted as a partial registry-based indicator rather than a comprehensive assessment of comorbidity burden, and residual confounding is likely.

The greater burden of adverse outcomes among older adults likely reflects not only chronological age and immunosenescence, but also the accumulation of age-related risk factors and multimorbidity. Because obesity/BMI and several other major comorbidities were not available in the registry, the observed age effect may capture part of the burden of unmeasured obesity and broader multimorbidity associated with older age.

The protective effect of vaccination observed in this study aligns with extensive global evidence demonstrating reduced risk of severe COVID-19, hospitalization and death among vaccinated individuals [24]. A meta-analysis involving more than 1.3 million individuals

also confirmed a significantly lower incidence of severe disease among vaccinated versus unvaccinated persons across different vaccine types [25].

Although male sex has been associated with an increased risk of hospitalization and death in several studies [21,26], this association was not identified in our cohort. This discrepancy should be interpreted cautiously, as only 20 hospitalization/death events occurred in the present dataset, substantially limiting statistical power and increasing the likelihood of type II error. Thus, the absence of a significant sex-related association in our analysis should not be interpreted as evidence of no true sex difference.

An additional key finding of this study was the strong association between demographic and clinical factors and vaccination status. Higher vaccination rates among older adults and individuals with underlying conditions may reflect increased risk perception and willingness to adhere to preventive measures. Urban residents also demonstrated higher vaccination uptake than those in rural areas. This difference is likely multifactorial and may reflect not only differences in access to healthcare services, but also socioeconomic conditions, health literacy, trust in health institutions, and perceived risk, none of which were available in the registry dataset. Seasonal variation in vaccination status, with higher rates during winter months, may reflect heightened public awareness during periods of increased viral circulation. These findings are consistent with previous research showing that age, socioeconomic status, education level and geographic region influence vaccine uptake [27]. A longitudinal survey from Sweden similarly found higher vaccination rates among older individuals, males and urban residents [28]. Collectively, these findings emphasize the need for interventions that enhance accessibility to vaccination services in rural areas and promote trust in vaccination among underserved population groups.

5. Limitations

This study has several limitations. First, all included SARS-CoV-2 diagnoses were based on rapid antigen testing performed within the PHC testing pathway; PCR-confirmed cases outside this pathway were not included in the present dataset. Although rapid testing reflected routine community practice, especially in later pandemic phases, reliance on antigen testing may have introduced diagnostic variability. This is particularly relevant for the early 2020–2021 period, when rapid tests were generally less sensitive than molecular assays and may have missed some lower-viral-load or asymptomatic infections. Second, the registry data did not allow us to reliably distinguish first infections from reinfections. As a result, repeated diagnoses for the same individual may have been recorded as separate events, which is especially important when interpreting findings from 2023–2024, when hybrid immunity from prior infection plus vaccination may have influenced clinical outcomes. Third, clinical severity among non-hospitalized patients (e.g., oxygen requirements, duration of symptoms) was not available, limiting the ability to differentiate the spectrum of disease severity within the outpatient population. Fourth, the registry captured only a limited set of comorbidities and did not include several major predictors of COVID-19 severity such as BMI/obesity, hypertension, broader cardiovascular disease, chronic respiratory disease, chronic kidney or liver disease, and cerebrovascular disease; therefore, residual confounding is likely. Fifth, only 20 hospitalization/death events occurred, limiting power for subgroup analyses and increasing the risk of type II error, particularly for variables such as sex. Sixth, socioeconomic factors such as education level, occupation and income were not recorded, although they are known to influence both vaccination behavior and health outcomes. Finally, this study reflects data from a single geographical area, which may affect the generalizability of findings to other regions.

6. Conclusions

This retrospective study conducted in Primary Healthcare settings in Giannitsa demonstrated that older age, the presence of registry-recorded underlying medical conditions and a lack of vaccination were the strongest predictors of hospitalization or death among adults diagnosed with SARS-CoV-2 infection. The epidemiological profile of COVID-19 shifted over time, with younger adults predominating during early pandemic years and older adults more affected in later phases, while vaccination coverage steadily increased and was highest among older individuals and those with comorbidities. These findings underscore the pivotal role of PHC in monitoring community-level epidemiological trends and highlight the importance of targeted public health interventions. Strengthening vaccination campaigns, particularly among high-risk individuals and residents of rural areas, improving accessibility to healthcare services outside urban centers and maintaining robust PHC-based surveillance systems can help reduce the burden of COVID-19 and enhance preparedness for future epidemics. Investing in PHC infrastructure and promoting equitable access to preventive care remain essential components of an effective long-term public health strategy.

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Institutional Review Board Statement: For the implementation of the study, approval was obtained from the Scientific Council of Primary Healthcare of the 3rd Health Region of Macedonia (approval number: 10561/26-02-2025, approved on 26 February 2025.).

Data Availability Statement: The datasets generated and analyzed during the current study are not publicly available because they contain anonymized registry-derived health data obtained from the National Registry of Patients with COVID-19 and linked national electronic health platforms. Access to these data is restricted by institutional and national data-protection regulations. De-identified data may be made available from the corresponding author upon reasonable request and subject to approval by the competent healthcare authority and applicable ethical and legal requirements.

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Conflicts of Interest: The authors declare no conflicts of interest.

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