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Original Research

Differences in the incidence and clinical outcomes of SARS-CoV-2 infection between Italian and non-Italian nationals using routine data

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ABSTRACT

Objectives: This study was to compare the incidence and clinical outcomes of SARS-CoV-2 infection between Italian and non-Italian nationals.
Study design: We retrospectively analysed data from the COVID-19 Italian integrated surveillance system (14 September 2020 to 17 October 2021).
Methods: We used multivariable Cox proportional hazards models to estimate the hazard ratio (HR) of infection and, among cases, the HRs of death, hospitalisation and subsequent admission to intensive care unit in non-Italian nationals relative to Italian nationals. Estimates were adjusted for differences in sociodemographic characteristics and in the week and region of diagnosis.
Results: Of 4,111,067 notified cases, 336,265 (8.2%) were non-Italian nationals. Compared with Italian nationals, non-Italians showed a lower incidence of SARS-CoV-2 infection (HR = 0.81, 95% confidence interval [CI]: 0.80–0.81). However, once diagnosed, they were more likely to be hospitalised (HR = 1.90, 95% CI: 1.87–1.92) and then admitted to intensive care unit (HR = 1.08, 95% CI: 1.04–1.13), with differences larger in those coming from countries with a lower human development index. Compared with Italian cases, an increased rate of death was observed in non-Italian cases from low–human development index countries (HR = 1.41, 95% CI: 1.23–1.62). The HRs of SARS-CoV-2 infection and severe outcomes slightly increased after the start of the vaccination campaign.
Conclusions: Underdiagnosis and delayed diagnosis in non-Italian nationals could explain their lower incidence compared with Italians and, among cases, their higher probability to present clinical conditions leading to worse outcomes. Facilitating early access to vaccination, diagnosis and treatment would improve the control of SARS-CoV-2 transmission and health outcomes in this vulnerable group.

Introduction

Several studies suggest that differences in cultural, behavioural and societal characteristics (e.g. socio-economic conditions, health-seeking behaviour and intergenerational cohabitation) make migrants and ethnic minority groups more exposed to the risk of SARS-CoV-2 infection and of severe COVID-19 compared with autochthonous populations.[1–4] However, these studies were mainly conducted among ethnic minority groups, individuals who were born and living in the host country since relatively long time, failing to capture the impact of the local epidemics on more recent migrants (economic migrants, refugees and asylum seekers), who are likely to experience a higher level of exposure to the risk of infection compared with the better integrated individuals from ethnic minority groups.[5] In fact, economic migrants, refugees, and asylum seekers are more likely to live in overcrowded accommodation and to be employed in precarious and low-skilled jobs

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associated with an increased risk of SARS-CoV-2 infection (e.g. care work, hospitality or construction)[6–8] and to be disproportionally affected by administrative, cultural and language barriers to healthcare access and to public health messaging.[9,10]

However, while migrants and ethnic minority group represent two different population groups in countries with a long migratory tradition, such as the United States and the United Kingdom, in countries where the migration process is recent, such as in Italy, these population groups partly overlap. In fact, in Italy, there was not a notable immigration flow until the 1980s, after which it progressively increased.[11]

In Italy, where almost 5.2 million foreign citizens were estimated to be living in January 2021 (8.7% of the total resident population),[12] we previously analysed, during the first epidemic wave (20 February to 19 July 2020), the difference in COVID-19–related clinical outcomes between Italian and non-Italian nationals (i.e. people with a reported non-Italian nationality, regardless of citizenship or country of birth).[13] This study showed an increased risk of hospitalisation and admission to intensive care unit (ICU) in non-Italian nationals compared with Italian nationals, as well as an increased risk of death in non-Italian nationals from countries with a low human development index (HDI).

The present study aims to integrate and update the previous analysis by comparing the incidence and clinical outcomes of SARS-CoV-2 infection between Italian and non-Italian nationals using the much larger data set of cases tested positive in the period from 14 September 2020 to 17 October 2021, who account for 94% of all cases notified in Italy since the start of the epidemic.

Methods

Data sources

We used data retrieved from the Italian national COVID-19 surveillance system, coordinated by the Italian Institute of Health, including information on the demographic and clinical characteristics and outcomes of all cases of SARS-CoV-2 infection that were laboratory confirmed by real-time polymerase chain reaction or, since 15 January 2021, detected also through an approved antigenic test (2% of cases notified up to 17 October 2021).[14] Data are collected daily using a secure online platform and checked for out-of-range values, inconsistencies, and duplicated records. The coordinating centre routinely sends a list of possible errors to regions for verification and possible corrections. We used the data set of notifications updated on 16 December 2021 and selected all cases of SARS-CoV-2 infection tested positive from 14 September 2020 to 17 October 2021 to allow at least 30 days of follow-up and 1 month of possible delay in notification of hospitalisation, admission to ICU, and death.

We also used information about the distribution of the Italian resident population in the year 2021 by citizenship (Italians vs documented foreigners as a whole), municipality of residence, sex, and age retrieved from the data sets publicly available at the Italian National Institute of Statistics (Istat) website.[12]

Information about the level of social and material vulnerability of the municipality of residence was retrieved from the *8milaCensus* platform managed by Istat.[15] This multidimensional indicator, updated to 2011, reflects contextual phenomena, measured at municipality level, that could have affected viral circulation in the community and partly individual exposure to the risk of SARS-CoV-2 infection and related outcomes (i.e. housing conditions, family size and composition, family economic discomfort, housing overcrowding, youth employment rate and welfare discomfort of families). Finally, we also used information about the level of urbanisation of the municipality of residence provided by Istat.[16] We linked these data sets through a deterministic record linkage using the municipality code as key variable.

Exposure, outcomes and potential confounders

Among all notified cases of SARS-CoV-2 infection, we defined as non-Italian nationals those reporting a non-Italian nationality, regardless of citizenship or country of birth. Nationality was classified as Italian vs non-Italian in general, and according to the 2019 HDI of the country of origin.[17] Based on the tertiles of the world's countries' HDI distribution, we distinguished among non-Italian nationals from low-HDI countries (HDI $\leq$0.664), medium-HDI countries (0.664 < HDI $\leq$ 0.809), and high-HDI countries (HDI >0.809).

We analysed the associations between nationality (exposure) and different SARS-CoV-2–related end points. First, among the whole population without an infection before the starting date of the study period, we compared the incidence of SARS-CoV-2 infection, assuming it as occurred at the date of testing positive, between Italian nationals and non-Italian nationals. We then compared the death rate in all detected cases of SARS-CoV-2 infection. We considered as COVID-19–associated deaths any notified person who died within 30 days from testing positive and, according to indications from the World Health Organization, who was presenting a clinical picture suggestive of COVID-19, in the absence of a clear cause of death different from COVID-19 (e.g. trauma) and in the absence of a complete clinical recovery from the disease.[18] Finally, we compared the hospitalisation rate and, among cases who were hospitalised, the rate of admission to intensive care unit (ICU) within 30 days since testing positive for SARS-CoV-2 infection.

The analysis was conducted taking into account as potential confounders of the relationship between nationality and outcomes the following variables: sex, age (categorised as <30 years, 5-year age groups from 30–34 to 70–74, and $\geq$75 years), Italian region of diagnosis (19 regions and two autonomous provinces), social and material vulnerability index of the municipality of residence (i.e. four categories based on quartiles of the index distribution weighted by municipality population size), level of urbanisation of the municipality of residence (i.e. urban, semiurban, and rural), and calendar week of diagnosis.

Statistical analysis

Of all notified cases of SARS-CoV-2 infection tested positive between 14 September 2020 and 17 October 2021, we excluded from the analysis those imported from abroad. We also excluded cases with missing or inconsistent dates of death, hospitalisation, or admission to ICU. Finally, we excluded cases with missing information about age, level of social and material vulnerability of the municipality of residence, and nationality, thus leaving only records with complete information for all outcomes and sociodemographic characteristics available for the analysis (Fig. 1).

We described the main sociodemographic characteristics by nationality using counts with percentages and median with interquartile range (IQR) for categorical and continuous variables, respectively.

We conducted a time-to-event analysis to evaluate the association between nationality and time to SARS-CoV-2 infection using the 14 September 2020 as the index date to calculate the length of follow-up, measured as the number of days elapsed from the index date to the date of infection or to 17 October 2021 for those uninfected.

Time-to-event analyses were also conducted among cases of SARS-CoV-2 infection to evaluate the association of nationality

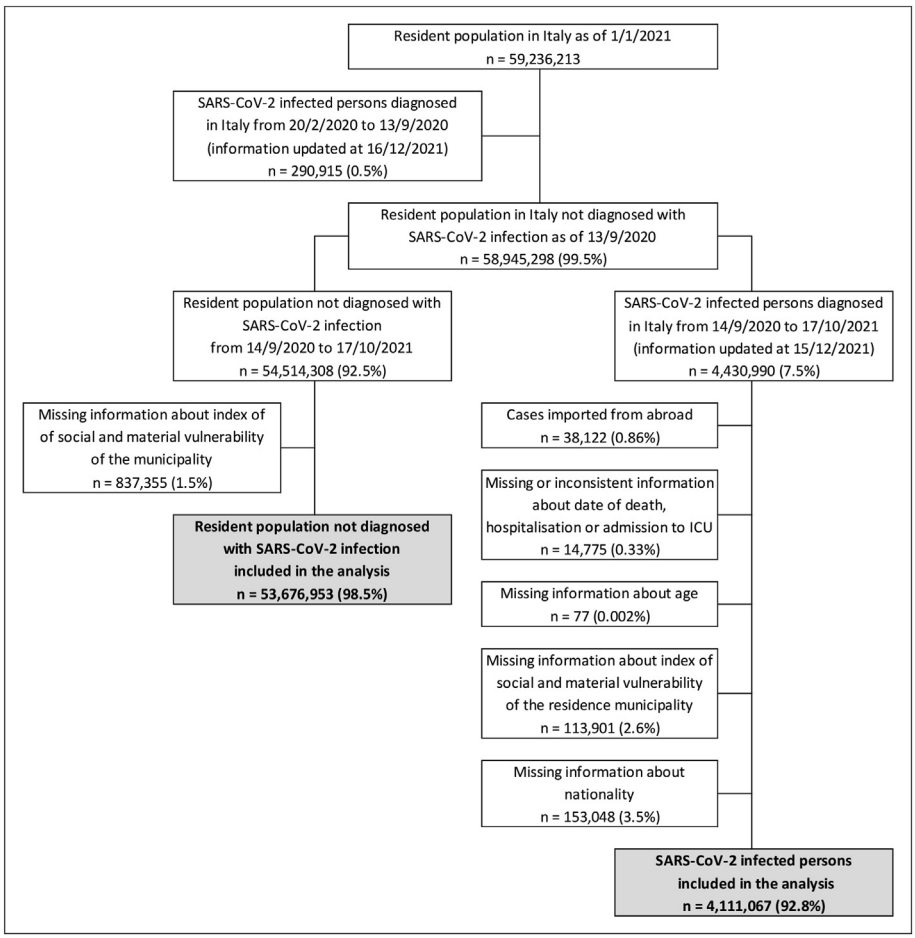

Fig. 1. Selection of the population included in the study. ICU, intensive care unit.

with time to COVID-19–associated death and hospitalisation and time to admission to ICU in hospitalised cases. The length of follow-up was measured as the number of days elapsed from the date of SARS-CoV-2 infection to the date of the event. Cases who did not experience the event were censored 30 days after the diagnosis of SARS-CoV-2 infection or, for the analysis of hospitalisation and admission to ICU, on the date of death if occurred earlier. We considered as died and hospitalised 0.5 days after infection all cases who were reported to have died and to have been hospitalised on the date of testing positive or within a week before it ($n = 1861$ 2.4% of deaths; $n = 125{,}798$, 41.0% of hospitalisations).

We used multivariable Cox proportional hazard models to estimate the adjusted hazard ratios (HRs) of SARS-CoV-2 infection, death, hospitalisation, and admission to ICU for non-Italian nationals compared with Italian nationals. All estimates were presented together with their 95% confidence interval (CI).

We tested the interaction between nationality and the epidemic phase through the likelihood ratio test and conducted a stratified analysis distinguishing between the epidemic phase before and after 31 January 2021. This is the date when the vaccination campaign, started in Italy on 27 December 2020, is expected to have had an impact.[19] In fact, the first second doses of the Comirnaty vaccine (the first authorised vaccine in Italy) were administered on 17 January 2021, and considering a time interval of 14 days needed to induce a full immune response, the first individuals potentially protected by a primary vaccination cycle were expected on 1 February 2021.

Finally, we conducted a sensitivity analysis using the country of birth instead of nationality to assess differences in the HRs of death, hospitalisation, and admission to ICU for foreign-born cases compared with cases born in Italy. It was not possible to evaluate differences in the incidence of SARS-CoV-2 infection because information on the population size by country of birth was unavailable.

The analyses were performed using Stata/SE version 16.1 (Stata Corp LLC, Texas, USA).

Results

Of all the 4,430,990 notified cases of SARS-CoV-2 infection tested positive between 14 September 2020 and 17 October 2021, we excluded from the analysis 38,122 (0.86%) cases imported from abroad (Fig. 1). We also excluded 14,775 (0.33%) cases with missing or inconsistent dates of death, hospitalisation, or admission to ICU. Finally, we excluded cases with missing information about age ($n = 77$; 0.002%), level of social and material vulnerability of the municipality of residence ($n = 113{,}901$; 2.6%), and nationality ($n = 153{,}048$; 3.5%), thus leaving 4,111,067 (92.8%) cases with complete information for all outcomes and sociodemographic characteristics available for the analysis. Finally, among the 54,510,982 residents in Italy who were not diagnosed with SARS-CoV-2 infection during the study period, we excluded 834,366 (1.5%) individuals living in municipalities with missing information on the level of social and material vulnerability.

Sociodemographic characteristics and time of infection

Cases of SARS-CoV-2 infection in non-Italian nationals from low-HDI countries ($n = 55{,}471$; 16.5%) were almost all from Asia

(n = 30,518; 55.0%) and south-central Africa (*n* = 24,230; 43.7%; Supplementary Fig. S1). Non-Italian cases from medium-HDI countries (*n* = 190,264; 56.6%) were mainly from European countries outside the European Union (*n* = 77,477; 40.7%), North Africa (*n* = 44,696; 23.5%), and south-central America (*n* = 41,837; 22.0%), whereas non-Italians from European Union countries (*n* = 73,975, 81.7%) accounted for most of cases from high-HDI countries (*n* = 90,530; 26.9%).

Cases of SARS-CoV-2 infection in non-Italian nationals were more frequently females (*n* = 178,159, 53.0%) compared with those in Italian nationals (*n* = 1,916,070, 50.8%), except cases from low-HDI countries who were more frequently males (*n* = 37,269, 67.2%) and relatively younger (median age: 34 years; IQR: 25–44) compared with cases in both Italian nationals (median age: 45 years; IQR: 26–60) and the whole group of non-Italian nationals (median age: 40 years; IQR: 28–50; Table 1).

Cases of SARS-CoV-2 infection in non-Italian nationals were more frequently reported in northern Italy (*n* = 254,644; 75.7%) and in urban areas (*n* = 151,965; 45.2%) compared with Italian cases (*n* = 1,947,948 [51.6%] and 1,406,421 [37.3%], respectively), particularly those in non-Italian nationals from medium and low-HDI countries. Compared with Italian cases, those in non-Italian nationals were rarely reported in municipalities with a high level of social and material vulnerability (*n* = 21,895 [6.5%] vs *n* = 1,052,476 [27.9%]).

Finally, compared with Italian cases (*n* = 1,784,181; 47.3%), those in non-Italian nationals were more frequently diagnosed during the epidemic phase following the implementation of the vaccination campaign in Italy (*n* = 177,479; 52.8%). The epidemiological curves presented in Fig. 2 show that this difference was particularly pronounced in the latest months of the study period from August to October 2021 (weeks 31–41).

Incidence and clinical outcomes of SARS-CoV-2 infection

The adjusted HR of infection presented in Table 2 show that compared with Italian nationals, non-Italian nationals as a whole had a reduced risk of SARS-CoV-2 infection (adjusted HR = 0.81, 95% CI: 0.80–0.81).

By contrast, once diagnosed, they showed an increased risk of hospitalisation (HR = 1.90, 95% CI: 1.87–1.92) and, in those hospitalised, an increased risk of admission to ICU (HR = 1.08, 95% CI: 1.04–1.13). The hazard of death among cases did not differ between the two groups (HR = 1.03, 95% CI: 0.97–1.08), although it was

Table 1
Sociodemographic characteristics of the overall population and of SARS-CoV-2–infected cases diagnosed in Italy from 14 September 2020 to 17 October 2021.

Sociodemographic characteristics	Italian nationals				Non-Italian nationals				Non-Italians from low-HDI countries		Non-Italians from medium-HDI countries		Non-Italians from high-HDI countries	
	Population	%	Cases	%	Population	%	Cases	%	Cases	%	Cases	%	Cases	%
Total	52,708,701	100.0	3,774,802	100.0	5,079,319	100.0	336,265	100.0	55,471	100.0	190,264	100.0	90,530	100.0
Sex														
Female	27,033,641	51.3	1,916,070	50.8	2,598,342	51.2	178,159	53.0	18,202	32.8	104,554	55.0	55,403	61.2
Male	25,675,060	48.7	1,858,732	49.2	2,480,977	48.8	158,106	47.0	37,269	67.2	85,710	45.0	35,127	38.8
Age group														
<15 years	6,588,262	12.5	434,788	11.5	896,278	17.6	23,652	7.0	4196	7.6	12,947	6.8	6509	7.2
15–19 years	2,577,291	4.9	230,036	6.1	219,879	4.3	13,992	4.2	2723	4.9	7929	4.2	3340	3.7
20–24 years	2,556,079	4.8	231,330	6.1	336,301	6.6	24,064	7.2	6387	11.5	12,457	6.5	5220	5.8
25–29 years	2,563,257	4.9	227,264	6.0	413,416	8.1	29,713	8.8	7334	13.2	16,508	8.7	5871	6.5
30–34 years	2,622,462	5.0	221,707	5.9	530,412	10.4	36,284	10.8	7349	13.2	20,141	10.6	8794	9.7
35–39 years	2,839,989	5.4	226,748	6.0	561,485	11.1	40,151	11.9	7229	13.0	22,849	12.0	10,073	11.1
40–44 years	3,362,928	6.4	259,867	6.9	548,066	10.8	42,368	12.6	6752	12.2	23,273	12.2	12,343	13.6
45–49 years	4,115,110	7.8	321,371	8.5	460,958	9.1	38,313	11.4	5054	9.1	21,482	11.3	11,777	13.0
50–54 years	4,311,285	8.2	331,292	8.8	385,371	7.6	32,719	9.7	3570	6.4	18,317	9.6	10,832	12.0
55–59 years	4,228,349	8.0	308,309	8.2	277,795	5.5	23,117	6.9	2286	4.1	13,961	7.3	6870	7.6
60–64 years	3,640,468	6.9	232,526	6.2	203,110	4.0	15,084	4.5	1328	2.4	9519	5.0	4237	4.7
65–69 years	3,263,963	6.2	179,240	4.7	118,770	2.3	7869	2.3	589	1.1	5276	2.8	2004	2.2
70–74 years	3,288,133	6.2	169,178	4.5	65,031	1.3	3925	1.2	274	0.5	2658	1.4	993	1.1
≥75 years	6,751,125	12.8	401,146	10.6	62,447	1.2	5014	1.5	400	0.7	2947	1.5	1667	1.8
Median age (IQR)	49	(27–65)	45	(26–60)	36	(22–48)	40	(28–50)	34	(25–44)	40	(29–51)	42	(31–51)
Level of urbanisation[a]														
Urban	18,557,114	35.2	1,406,421	37.3	2,238,480	44.1	151,965	45.2	24,602	44.4	92,983	48.9	34,380	38.0
Semiurban	25,405,107	48.2	1,810,695	48.0	2,180,242	42.9	145,264	43.2	24,161	43.6	78,120	41.1	42,983	47.5
Rural	8,746,480	16.6	557,686	14.8	660,597	13.0	39,036	11.6	6708	12.1	19,161	10.1	13,167	14.5
Level of social and material vulnerability[a]														
Low	6,571,273	12.5	532,719	14.1	554,080	10.9	44,534	13.2	6438	11.6	23,426	12.3	14,670	16.2
Medium-low	11,482,259	21.8	906,761	24.0	1,303,275	25.7	105,513	31.4	18,163	32.7	58,997	31.0	28,353	31.3
Medium-high	19,116,265	36.3	1,282,846	34.0	2,396,879	47.2	164,323	48.9	25,971	46.8	98,466	51.8	39,886	44.1
High	15,538,904	29.5	1,052,476	27.9	825,085	16.2	21,895	6.5	4899	8.8	9375	4.9	7621	8.4
Geographical macroarea of Italy														
North-West	13,938,966	26.4	1,054,776	27.9	1,760,765	34.7	136,260	40.5	19,976	36.0	82,939	43.6	33,345	36.8
North-East	10,063,788	19.1	893,172	23.7	1,282,328	25.2	118,384	35.2	22,140	39.9	64,763	34.0	31,481	34.8
Centre	10,428,111	19.8	697,468	18.5	1,296,284	25.5	69,309	20.6	10,725	19.3	37,597	19.8	20,987	23.2
South and Islands	18,277,836	34.7	1,129,386	29.9	739,942	14.6	12,312	3.7	2630	4.7	4965	2.6	4717	5.2
Period of diagnosis (epidemic phase)														
Phase 1 (14 September 2020–31 January 2021)	NA	NA	1,990,621	52.7	NA	NA	158,786	47.2	28,280	51.0	89,733	47.2	40,773	45.0
Phase 2 (1 February 2021 to 17 October 2021)	NA	NA	1,784,181	47.3	NA	NA	177,479	52.8	27,191	49.0	100,531	52.8	49,757	55.0

HDI, human development index; IQR, interquartile range; NA, not applicable.
[a] The level of urbanisation and the level of social and material vulnerability refer to the municipality of residence.

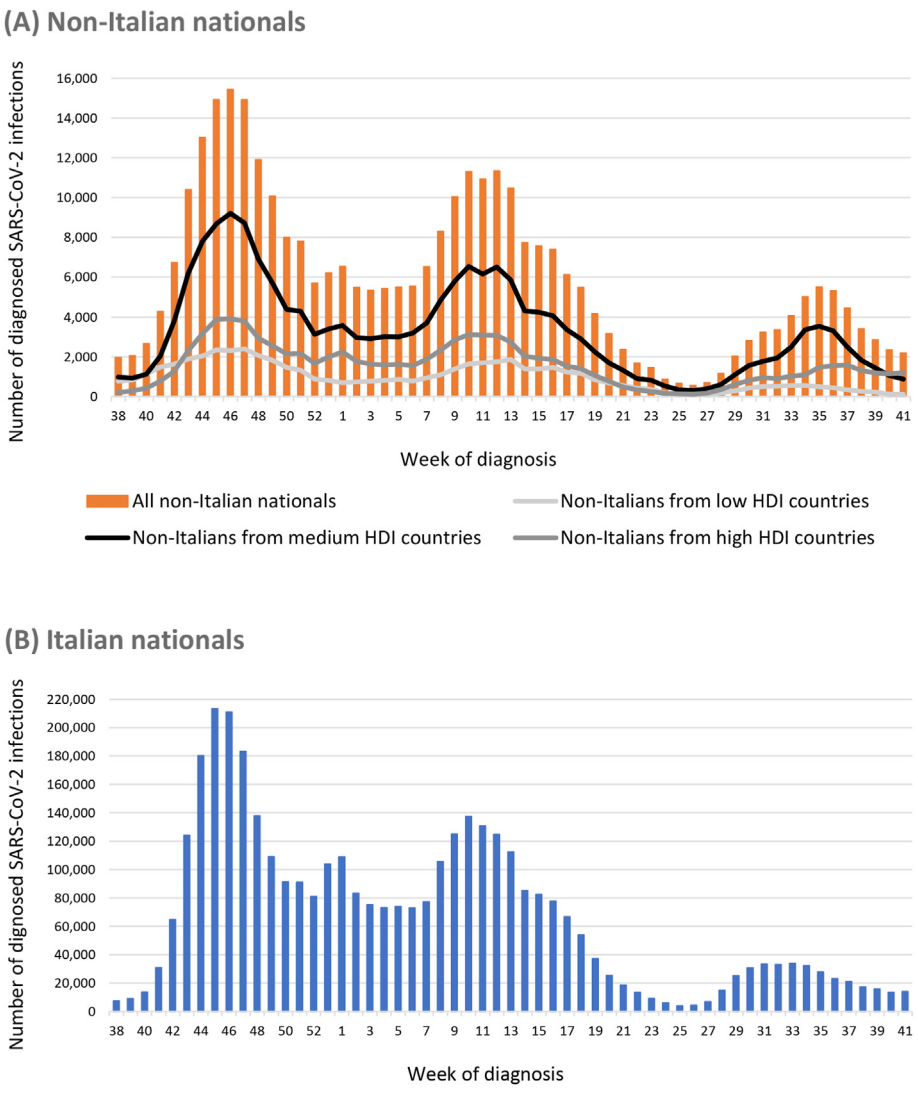

Fig. 2. SARS-CoV-2 infection epidemiological curves in non-Italian nationals (A) and Italian nationals (B), week 38/2020 (14–20 September) to week 41/2021 (11–17 October). HDI, human development index.

increased in non-Italian cases from low-HDI countries (HR = 1.41, 95% CI: 1.23–1.62). In general, all the considered clinical outcomes among cases showed an inverse gradient by which the hazard of these events increased as the HDI level of the country of origin decreased.

We found an interaction between nationality and the epidemic phase for all the considered events (likelihood ratio tests, $P < 0.05$). The analysis stratified by epidemic phase presented in Fig. 3 showed how, relative to Italian nationals, the risk of all events in non-Italian nationals slightly increased from the first period (from 14 September 2020 to 31 January 2021) to the second period following the implementation of the COVID-19 vaccination campaign in Italy (from 1 February to 17 October 2021).

The sensitivity analysis conducted using the country of birth instead of nationality as exposure variable showed very similar results (Supplementary Table S1).

Discussion

We found that non-Italian nationals were less likely to be diagnosed with SARS-CoV-2 infection compared with the Italian population. Once diagnosed, however, they were more likely to be hospitalised and to be admitted to ICU, also showing a higher risk of COVID-19–associated death in those from low-HDI countries. The risks of hospitalisation, admission to ICU, and death were found to increase with decreasing HDI of the country of origin. We also found that, relative to Italian nationals, the risk of infection, death, hospitalisation, and admission to ICU slightly increased after the implementation of the COVID-19 vaccination campaign in Italy (from 1 February to 17 October 2021).

It is possible that non-Italian nationals were at lower risk of infection because of the smaller social networks that migrants have been described to experience.[20] However, this would not explain why when diagnosed, non-Italian cases showed worse clinical outcomes than their Italian counterpart. For this reason, we believe it is more likely that non-Italian nationals were not at lower risk of being infected but rather less likely to be diagnosed unless the disease progressed to more severe symptoms requiring hospitalisation. This hypothesis is supported by findings from a seroprevalence survey conducted in a social housing neighbourhood in Milan, northern Italy, showing a prevalence of SARS-CoV-2 antibodies in non-Italians about twice that in Italians.[24] Underdiagnosis in non-Italian nationals could be partly explained by the fact that in Italy, although all non-Italian nationals have free access to

Table 2
Hazard ratio of diagnosis with SARS-CoV-2 infection and subsequent death, hospitalisation and admission to ICU by nationality.

Diagnosis of SARS-CoV-2 infection	Population	Cases	PD	Incidence per 100,000 PD	Crude HR	(95% CI)	Adjusted HR[a]	(95% CI)
Nationality (1)								
Italian	52,708,701	3,774,802	20,069,606,450	18.8	Ref.		Ref.	
Non-Italian	5,079,319	336,265	1,946,192,112	17.3	0.92	(0.92–0.92)	0.81	(0.80–0.81)
Death	**Cases**	**Deaths**	**PD**	**Death rate per 100,000 PD**	**Crude HR**	**(95% CI)**	**Adjusted HR[a]**	**(95% CI)**
Nationality (1)								
Italian	3,774,802	74,781	111,928,756	66.8	Ref.		Ref.	
Non-Italian	336,265	1511	10,062,137	15.0	0.23	(0.21–0.24)	1.03	(0.97–1.08)
Nationality (2)								
Italian	3,774,802	74,781	111,928,756	66.8	Ref.		Ref.	
Low-HDI countries	55,471	202	1,660,556	12.2	0.18	(0.16–0.21)	1.41	(1.23–1.62)
Medium-HDI countries	190,264	907	5,692,805	15.9	0.24	(0.22–0.25)	1.00	(0.94–1.07)
High-HDI countries	90,530	402	2,708,776	14.8	0.22	(0.20–0.25)	0.95	(0.86–1.05)
Hospitalisation	**Cases**	**Hospitalised patients**	**PD**	**Hospitalisation rate per 100,000 PD**	**Crude HR**	**(95% CI)**	**Adjusted HR[a]**	**(95% CI)**
Nationality (1)								
Italian	3,774,802	278,741	105,481,161	264.3	Ref.		Ref.	
Non-Italian	336,265	28,256	9,303,341	303.7	1.15	(1.13–1.16)	1.90	(1.87–1.92)
Nationality (2)								
Italian	3,774,802	278,741	105,481,161	264.3	Ref.		Ref.	
Low-HDI countries	55,471	5912	1,496,539	395.0	1.48	(1.44–1.52)	2.88	(2.81–2.96)
Medium-HDI countries	190,264	16,728	5,245,203	318.9	1.20	(1.18–1.22)	1.90	(1.87–1.93)
High-HDI countries	90,530	5616	2,561,600	219.2	0.84	(0.82–0.86)	1.41	(1.38–1.45)
Admission to ICU	**Hospitalised cases**	**Admitted to ICU**	**PD**	**ICU admission rate per 100,000 PD**	**Crude HR**	**(95% CI)**	**Adjusted HR[a]**	**(95% CI)**
Nationality (1)								
Italian	278,741	40,775	6,637,420	614.3	Ref.		Ref.	
Non-Italian	28,256	2871	763,321	376.1	0.66	(0.64–0.69)	1.08	(1.04–1.13)
Nationality (2)								
Italian	278,741	40,775	6,637,420	614.3	Ref.		Ref.	
Low-HDI countries	5912	479	163,556	292.9	0.52	(0.48–0.57)	1.09	(0.99–1.19)
Medium-HDI countries	16,728	1765	451,098	391.3	0.69	(0.65–0.72)	1.10	(1.04–1.15)
High-HDI countries	5616	627	148,667	421.7	0.73	(0.68–0.79)	1.05	(0.97–1.13)

CI, confidence interval; HDI, human development index; HR, hazard ratio; ICU, intensive care unit; PD, person-days; ref., reference category.
[a] Adjusted for sex, age, geographical region of diagnosis, level of urbanisation of the municipality of residence, level of social and material vulnerability of the municipality of residence and calendar week of diagnosis.

emergency services and some outpatient services,[21] only documented immigrants have access to additional services, including the assignment to a general practitioner, who is the most likely mediator for diagnosis. Moreover, informal barriers (language, administrative, cultural, and social) might have hindered the access to healthcare services regardless of status.[9,10] It is worthwhile to note that in Italy, in January 2021, the case definition for surveillance purposes was extended to include cases who were laboratory confirmed through an antigenic test. The execution of this kind of test was also made available for pay in pharmacies and laboratories outside the public circuit,[22] thus facilitating the access to diagnosis, especially where public services were overcrowded. The access to this diagnostic service, however, was likely higher in Italian nationals compared with non-Italian nationals, the former being probably more informed about the service and more prone to sustain its cost. This possibly led to a more pronounced increase in the number of diagnosed infections, especially those asymptomatic or paucisymptomatic, in Italian nationals compared with non-Italians. Finally, non-Italian nationals, particularly those engaged in precarious works, might have avoided diagnosis fearing the isolation/quarantine and the consequent impact on their economic income.[23]

All this suggests that non-Italian nationals infected with SARS-CoV-2 were more likely to be undiagnosed or diagnosed less timely than Italian nationals, possibly when the disease was more advanced, thus explaining the increased risk of severe outcomes observed in non-Italian nationals, especially in those from low-HDI countries. This hypothesis is consistent with findings from a study conducted in northern Italy showing that immigrant women were more likely to be tested for SARS-CoV-2 infection only when presenting severe symptoms.[25] Overall, we did not observe a difference in the hazard of death between Italian and non-Italian nationals, although it was increased in non-Italian cases from low-HDI countries. This result is consistent with findings from a study conducted in Milan, northern Italy, where in-hospital mortality was found to not significantly differ between Italian and immigrant patients.[26]

A reduced access to vaccination could partly explain the slight increase in the HRs of infection and severe clinical outcomes in non-Italians compared with Italian nationals that was observed during the epidemic phase following the implementation of the vaccination campaign. Although the available data did not allow us to adequately assess the COVID-19 vaccination coverage by nationality, a recent study conducted in the metropolitan area of Milan in the Lombardy region showed, in the period January to September 2021, an estimated risk of missed vaccination in non-Italian nationals more than twice that estimated in Italian nationals, both overall and among individuals aged $\geq$50 years.[27] A lower COVID-19 vaccination coverage in migrants and ethnic minorities compared with the autochthonous population was also observed elsewhere in Europe.[8]

In general, our findings are consistent with those from other European countries. Although sometimes designed in different ways, studies conducted in Spain, Norway, Denmark, and Sweden

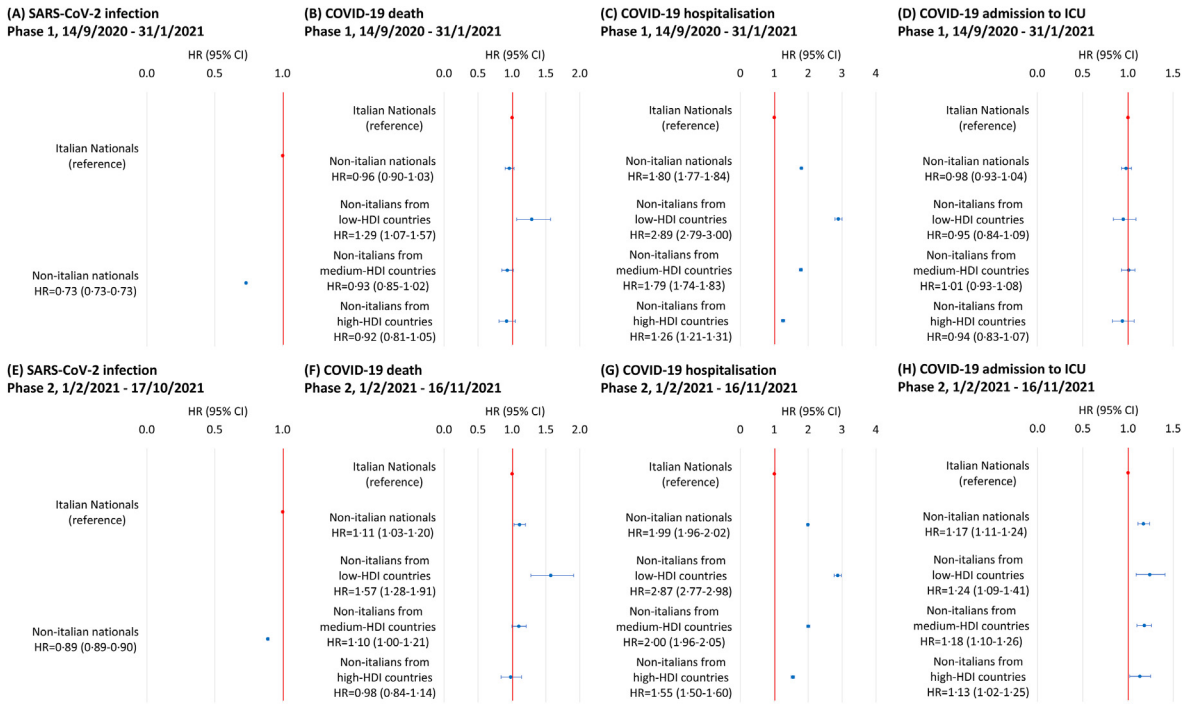

Fig. 3. Hazard ratio of SARS-CoV-2 infection and subsequent death, hospitalisation, and admission to ICU by nationality and epidemic phase. HR, hazard ratio adjusted for sex, age, geographical region of diagnosis, level of urbanisation of the municipality of residence, level of social and material vulnerability of the municipality of residence and calendar week of diagnosis; CI, confidence interval; HDI, human development index; ICU, intensive care unit.

also showed an increased risk of hospitalisation and admission to ICU due to COVID-19 in migrants compared with autochthonous populations.[28–31] In Norway, it was observed a higher rate of hospitalisation in cases born abroad compared with those born in Norway (4.7% vs 3.2%),[28] and in Madrid, Spain, an increased risk of admission to ICU in hospitalised patients from non-European countries compared with those from European countries (odds ratio adjusted for age/gender = 1.43, 95% CI: 1.03–1.98).[29] In Denmark, it was observed a higher proportion of non-Western migrants (15%) in COVID-19–hospitalised cases than in the general population (9%),[30] and in Sweden, among the whole population, a higher rate of admission to ICU in foreign-born persons compared with natives.[31] Consistently with our findings on lethality, a stratified analysis from Sweden showed an increased risk of COVID-19–associated death in migrants from low- or middle-income countries compared with nationals,[32] whereas no excess mortality by migrant status was observed in Denmark.[30] However, in contrast with findings from these countries, we did not observe an increased risk of SARS-CoV-2 infection in non-nationals compared with nationals. As discussed previously, this could be explained by a higher rate of missed diagnosis in non-Italian cases compared with Italian cases, especially in those asymptomatic or paucisymptomatic, possibly leading to estimates of severe clinical outcomes in this population group greater than elsewhere.

Our study has the strength to be highly representative of the population living in Italy, including all cases of SARS-CoV-2 infection notified to the national surveillance system over more than 1 year.

However, this analysis also has some limitations. Differences in the incidence of SARS-CoV-2 infection should be interpreted with caution because the population size at risk to develop the disease was assessed using estimates of the population residing in Italy at the beginning of the year 2021. Therefore, it does not account for deaths unrelated to COVID-19 that occurred thereafter, as well as for population movements to/from abroad that, given their higher mobility, are expected to have been more frequent among foreigners than among Italians.

It was not possible to adjust our estimates for the presence of pre-existing comorbidities since this information was available only for 58% of all the cases notified to the Italian integrated surveillance system. However, based on data from the six Italian regions where the percentage of missing information about pre-existing comorbidities was below 5% (accounting for 2,220,194 [54%] of the notified cases included in the study), the models adjusted for the presence of comorbidities yielded estimates of the HRs of severe clinical outcomes in non-Italian nationals compared with Italian nationals very close to those presented in the main analysis (Supplementary Table S2).

Finally, we cannot adjust for individual socio-economic conditions nor stratify the analysis grouping non-Italian nationals by length of stay in Italy, both factors likely affecting COVID-19–associated morbidity and mortality. Although we adjusted the analysis for social and material vulnerability measured at municipality level, this indicator may suffer from ecological fallacy, given that, especially in large municipalities, the contextual social and material vulnerability may differ among subareas and poorly reflect individual conditions. In conclusion, the results suggest that, in Italy, there was both underdiagnosis and delayed diagnosis of SARS-CoV-2 infection in non-Italian nationals compared with the autochthonous population, possibly explaining the lower incidence but worse clinical outcomes in this population group. If non-nationals are hindered in accessing healthcare services in a timely manner, vaccination, diagnosis, and treatment can be in turn delayed with a possible negative impact on individual outcome as well as on disease prevention and control at population level. Removing healthcare access barriers is, therefore, essential to control SARS-CoV-2 transmission, preserve health services, and improve the health outcomes in this vulnerable group as well as in the whole population living in Italy.

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Ethical approval

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Competing interests

None declared.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.puhe.2022.07.022.

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