Title: **Prevalence of SARS-CoV-2 (COVID-19) in Italians and in Immigrants in Northern Italy.**

Prevalenza di infezione SARS-CoV-2 (COVID-19) negli Italiani e negli immigrati in Nord Italia.

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Abstract

It has been hypothesized that bacille Calmette-Guerin (BCG) vaccine can be protective against COVID-19.

We report that immigrants resident in Reggio Emilia province, mostly coming from countries with high BCG vaccination coverage, and Italians had a similar prevalence of infection (OR 0.99; 95 % confidence interval [CI] 0.82-1.2) and similar probability of being tested (OR 0.93; 95% CI 0.81-1.1).

Our data do not support the hypothesis that immigrants from countries where BCG vaccination is recommended have a lower risk of COVID-19 infection.

È stato ipotizzato che la vaccinazione con bacillo Calmette-Guerin (BCG) possa conferire una protezione verso l'infezione da COVID-19.

Non abbiamo trovato differenze nella prevalenza di infezione (OR 0.99; intervallo di confidenza al 95% [95%CI] 0.82-1.2) e nella probabilità di essere testati (OR 0.93; 95%CI 0.81-1.1) fra gli italiani e negli immigrati, provenienti in gran parte da paesi dove il BCG è raccomandato, in Provincia di Reggio Emilia.

I nostri dati non supportano l'ipotesi che immigrati da paesi dove il vaccino BGC è raccomandato siano a minor rischio di infezione per COVID-19.

Key words: SARS-CoV-2 (COVID-19); migrant health; women's health; BCG vaccine

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The SARS-CoV-2 (COVID-19) epidemic is spreading throughout northern Italy (1-4).

It has been hypothesized that immigrants from low-income countries may be at lower risk of being infected and/ or of reporting symptoms than native-born individuals. The hypothesis comes from the observation that absolute numbers of foreigners among people presenting with symptoms are apparently lower than expected based on the percentage of immigrant population. The bacille Calmette-Guerin (BCG) vaccine for tuberculosis (TB) disease has been hypothesized as a possible protective factor in immigrants coming from countries with a high prevalence of TB since in many of these countries BCG coverage is high. BCG vaccine has proved to be effective not only in preventing TB, but also in stimulating the innate immune system response to other infectious agents and neoplasia (5-8). This led to starting clinical trials of vaccinating healthcare workers and the general population (9,10).

It is important to note that the age distribution of resident immigrants and Italians in northern Italy is very different, with immigrants being much younger than Italians. It is therefore difficult to determine whether there is a real difference in risk underlying the lower-than-expected absolute number.

Furthermore, despite a universal healthcare system providing urgent and preventive care for free to all the resident population, regardless of citizenship, immigrants may experience more difficulties in accessing healthcare services (11-13). It is thus possible that COVID-19 is underdiagnosed in this group.

In this short report we present the age- and sex-adjusted probability of being tested and of receiving a diagnosis of COVID-19 and the positive predictive value of the referral to swab in immigrants and Italians.

Setting

The province of Reggio Emilia is located in northern Italy and has 532,000 inhabitants, 66,000 of whom are foreigners, mostly from low-income countries (Table 1). The Italian healthcare system provides free healthcare for all acute care and for preventive measures.

In the Reggio Emilia Province, the first case of COVID-19 was diagnosed on February 27, 2020. Up to March 26, there were 1600 confirmed cases and the epidemic was still spreading.

Population

The reported analyses include all the resident population who have been tested for SARS-CoV-2 with PCR on naso- and oropharyngeal swab swabs. During the evolution of the epidemic, criteria for testing has changed; initially and up to the first week of March 2020, the Reggio Emilia Local Health Authority's Public Health Department and the hospital emergency rooms tested all suspected cases with flu-like symptoms, respiratory symptoms or fever as well as those who had had contact with a case or had been in one of the "red zones" where the initial cluster occurred. In this phase, all the asymptomatic close contacts of a positive case were also tested. In the subsequent phase, all symptomatic patients with symptoms suggestive of COVID-19 (flu-like symptoms, respiratory symptoms, syncope or fever) were tested regardless of whether they had had contact with a positive case but asymptomatic contacts were not tested further. In this analysis only symptomatic patients tested for COVID-19 have been included.

Data were retrieved from the databases of the tested people set up by the Local Health Authority's Public Health Department for surveillance and management purposes.

Statistical analyses

Here we report the number of individuals tested and the probability of being tested and the prevalence of positive tests per 1000 inhabitants by age (≤ 47 years; 48-60 years; > 60), sex and place of birth (Italy, abroad). As denominator for these two measures we used the resident population on 31/12/2019 (National Institute of Statistics – Istat). This data point allowed us to stratify individuals by citizenship and not by place of birth, which is pertinent as in Italy citizenship is determined by parents' citizenship and not by place of birth.

We also report the positive predictive value of the referral to swab, i.e., the percentage of positive tests among those tested, stratified by age, sex and place of birth.

Further, we report multivariate logistic regression for the three indicators, using age, sex and place of birth as covariate. We report stratified models for any strong interaction observed.

Results

From March 6 to March 26 2020, 2635 symptomatic people resident in the Reggio Emilia province were tested for SARS-CoV-2: of these, 215 (8.2%) were foreigners (Table 1).

The proportion of tested people among foreigners and Italians was similar when stratified by age and sex. The prevalence of positive tests in the resident population was also similar (Table 2).

The proportion of positive tests, i.e., the positive predictive value of the referral to swab, was higher in foreign women and slightly lower in Italian women compared to foreign and Italian males, respectively (Table 2).

Multivariate analyses confirm that the age- and sex-adjusted probability of being tested was similar in immigrants and Italians, as was the prevalence of positive tests. The adjusted probability of being positive was similar in immigrants and Italians, which increased with age; the probability was also higher for foreign women compared to foreign men, while in Italians the opposite was true (Table 3).

Discussion

Our results do not support the hypothesis of a lower incidence of SARS-CoV-2 infection in immigrants in the northern Italy epidemic. The observation is also corroborated by an identical probability of being tested.

The immigrant population in the Reggio Emilia province comes mostly from North Africa, Eastern Europe, China and South Asia (Table 4). These are all countries where BCG is recommended, even if the population coverage can vary greatly (14). We do not know the vaccine status of our positive cases or the BCG vaccine status of the foreign resident population, but it is surely higher than that of people born in Italy, where BCG vaccination has never been implemented. Other studies found a difference between Immigrants and natives in vaccine-related TB seroprevalence in high-income countries (15).

It is interesting that, even if the probability of being tested does not show any difference by place of birth or sex, we found a much higher probability of being positive once tested in immigrant women. This suggests that immigrant women undergo a swab only when symptoms are more predictive and probably severe. Reduced access to emergency services in immigrant women has already been observed in other studies focusing on various acute diseases (11-13). On the other hand, age seems to be a reason to undergo the test only with more predictive symptoms for Italians and immigrants, both males and females.

The main limitation of this short report is that we had different definitions of immigrant as denominator (citizenship) and as the numerator (place of birth). This limitation is particularly relevant for younger people,

given that in Italy citizenship is determined by the parents' citizenship and not by place of birth, although young adults born in Italy and still living in Italy at age 18 can apply for Italian citizenship. In COVID-19, as age < 18 is not relevant, this bias should not influence our estimates. Such approximation has been used in other studies on immigrant health in Italy (16).

In conclusion, immigrants and Italians have similar prevalence of COVID-19. Overall, the probability of being tested is similar, but our data suggest that immigrant women may have reduced access to swabs.

Table 1. Resident population, people tested for COVID-19 and people with positive test by age, sex and place of birth/nationality

Tabella 1. Popolazione residente, testati per COVID-19 e positivi al test per età, sesso, e luogo di nascita/nazionalità

	Population				Tested				Positives			
	Italians		immigrants		Italians		immigrants		Italians		immigrants	
	males	females	males	females	males	female	males	females	males	Females	males	females
≤ 47	125088	119765	25914	24112	251	339	45	61	131	132	12	31
48-60	47901	46698	4102	5988	311	276	34	32	205	164	24	28
> 60	60902	73641	1573	3975	732	511	22	21	491	319	12	15

Table 2. Probability of being tested, prevalence of positive COVID-19 tests and positive predictive value of the referral to swab, by age, sex and place of birth/nationality

Tabella 2. Probabilità di essere testati, prevalenza di positivi al COVID-19 e valore predittivo positivo dell'invio al tampone per età, sesso, e luogo di nascita/nazionalità

	probability of being tested (x1000)				prevalence of positive test (x1000)				positive predictive value of referral to swab %			
	Italians		immigrants		Italians		immigrants		Italians		immigrants	
	males	females	Males	females	males	females	males	females	males	Females	males	females
≤ 47	2.0	2.8	1.7	2.5	1.0	1.1	0.5	1.3	52.2	38.9	26.7	50.8
48-60	6.5	5.9	8.3	5.3	4.3	3.5	5.9	4.7	65.9	59.4	70.6	87.5
> 60	12.0	6.9	14.0	5.3	8.1	4.3	7.6	3.8	67.1	62.4	54.5	71.4

Table 3. Multivariate models for probability of being tested, prevalence of positive COVID-19 test and positive predictive value of the referral to swab.

Tabella 3. Modelli multivariati per la probabilità di essere testati, prevalenza di positivi al COVID-19 e valore predittivo positivo dell'invio al tampone.

	Probability of being tested		Prevalence of positive test		Positive predictive value					
					overall		Italians		immigrants	
	OR	CI 95%	OR	CI 95%	OR	CI 95%	OR	CI 95%	OR	CI 95%
age										
≤ 47	ref.		ref.		ref.		ref.		ref.	
48-60	2.6	(2.4-2.9)	3.9	(3.4-4.5)	2.3	(1.8-2.8)	2.0	(1.6-2.6)	6.5	(3.1-1.4)
> 60	3.9	(3.6-4.3)	5.9	(5.1-6.7)	2.3	(1.9-2.8)	2.2	(1.8-2.7)	2.8	(1.3-6.1)
sex										
male	ref		ref.		ref.		ref.		ref.	
female	0.81	(0.75-0.87)	0.71	(0.64-0.78)	0.81	(0.69-0.95)	0.74	(0.62-0.88)	2.7	(1.4-4.9)
nationality										
Italian	ref.		ref.		ref.					
immigrant	0.93	(0.81-1.1)	0.99	(0.82-1.2)	1.1	(0.83-1.5)				

Table 4. Foreign population resident in the Reggio Emilia province by country, 2018, National Institute of Statistics (Istat).

Tabella 4. Popolazione straniera residente nella provincia di Reggio Emilia per paese, 2018 (Istat).

	males	females	total
Morocco	3878	3615	7493
Romania	2508	3870	6378
Albania	3239	3065	6304
Pop Rep China	2935	2787	5722
India	2991	2611	5602
Pakistan	3107	2011	5118
Ukraine	908	3417	4325
Moldova	974	1961	2935
Ghana	1459	936	2395
Nigeria	1191	932	2123
Tunisia	1155	756	1911
Egypt	938	366	1304
Georgia	266	986	1252
Senegal	763	360	1123
Poland	232	818	1050
Sri Lanka	545	498	1043
Other	4500	5086	9586
Total	**31589**	**34075**	**65664**

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