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The experience of the health care workers of a severely hit SARS-CoV-2 referral Hospital in Italy: incidence, clinical course and modifiable risk factors for COVID-19 infection

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ABSTRACT

Background During the COVID-19 pandemic, the health care workers (HCWs) at the frontline have been largely exposed to infected patients, running a high risk of being infected by the SARS-CoV-2 virus. Since limiting transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in health care setting is crucial to avoid the community spread of SARS-CoV-2, we want to share our experience as an early hit hospital where standard infection control practices have been conscientiously applied and effective. We believe that our example, as first and hardest hit country, might be a warning and aid not only for those who have been hit later, but also for a second fearful wave of contagion. In addition, we want to offer an insight on modifiable risk factors for HWs-related infection.

Methods Demographic, lifestyle, work-related and comorbidities data of 1447 HCWs, which underwent a nasopharyngeal swab for SARS-CoV-2, were retrospectively collected. For the 164 HCWs positive for SARS-CoV-2, data about safety in the workplace, symptoms and clinical course of COVID-19 were also collected. Cumulative incidence of SARS-CoV-2 infection was estimated. Risk factors for SARS-CoV-2 infection were assessed using a multivariable Poisson regression.

Results The cumulative incidence of SARS-CoV-2 infection among the screened HCWs was 11.33% (9.72–13.21). Working in a COVID-19 ward, being a former smoker (versus being a person who never smoked) and BMI was positively associated with SARS-CoV-2 infection, whereas being a current smoker was negatively associated with this variable.

Conclusions Assuming an equal accessibility and proper use of personal protective equipment of all the HCWs of our Hospital, the great and more prolonged contact with COVID-19 patients remains the crucial risk factor for SARS-CoV-2. Therefore, increased and particular care needs to be focused specifically on the most exposed HCWs groups, which should be safeguarded. Furthermore, in order to limit the risk of asymptomatic spread of SARS-CoV-2 infection, the HCWs mild symptoms of COVID-19 should be considered when evaluating the potential benefits of universal staff testing.

Keywords COVID-19, health care workers, retrospective cohort study, risk of infection, SARS-CoV-2

Introduction

A novel strand of Coronavirus (SARS-CoV-2) is the cause of a severe, potentially fatal respiratory syndrome, which is currently known as COVID-19 and represents one of the most serious health emergencies of the 21st century.[1]

As of 23 September 2020, Italy had 302.537 confirmed cases. Among them, about 40% needed hospitalization and 16% of those needed to be admitted in an intensive care unit (ICU).[2,3]

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The country's financial hub, Lombardy, followed by other productive regions in Northern Italy such as Emilia-Romagna and Veneto, was the most impacted by the COVID-19 spread, and their hospitals struggled to cope.

Specifically, since the first indigenous case was confirmed on 21 February 2020, and admitted to our Hospital, Fondazione IRCCS Policlinico San Matteo of Pavia, Lombardy, it was appointed as a national SARS-CoV-2 referral center.[4,5] Since the beginning of the emergency, our Hospital recorded a total of 1.266 COVID-19 admissions with a number of 431 deceased.

Health care workers (HCWs) at the frontline have been restlessly fighting COVID-19, being exposed to infected patients for a hefty amount of hours per day. Since they are the first to care for infected patients, it seems reasonable that might as well be likely to be the first to contract the infection.[6]

In spite of the early, limited awareness of this new enemy, which has kneeled our clinic in the most critical period of the outbreak in Northern Italy, results in terms of infection among HWs has been positive. With this in mind, we want to offer an insight in to the epidemic management strategies and risk assessment of health-care worker exposure that we applied during the outbreak. Due to the not-aligned time of COVID-19 spread worldwide, we believe that these are going to be useful.

In addition, since data on HCWs real-life, individual clinical characteristics and risk factors for the infection are currently scarce, the study tries to fill at least part of this gap by reporting the epidemiological, clinical and lifestyle characteristics that might play roles in the susceptibility of HCWs to COVID-19.

Materials and methods

Study design, population and data collection

This is an observational retrospective cohort study carried out in the IRCCS Policlinico San Matteo of Pavia, Lombardy. From 22 February 2020, this Hospital was appointed as a COVID-19 referral center and its 4632 HCWs have been involved in this unprecedented health emergency.[4,5] Two sources of data were queried and are described below.

Data have been collected by medical direction in partnership with occupational medicine, which deals with the health surveillance of workers, and Nursing Direction. Before analysis, all data have been made anonymous.

Firstly, records of the 1447 HCWs, which underwent a nasopharyngeal swab for SARS-CoV-2 RNA detention from 22 February to 8 May 2020, were collected. These HCWs were the employees who were tested, in accordance to the Local Guidelines at the beginning of the pandemic, because they had symptoms suggestive of COVID-19 or because they had high-risk contacts with SARS-CoV-2-positive individuals. For each of these HCWs, we collected the demographic (age and gender) and occupational (length of service, job roles) characteristics using administrative databases, and we retrospectively collected the potential risk factors for COVID-19 infection such as lifestyle variables (BMI, smoking habit, alcohol consumption), work-related characteristics (work in COVID-19 wards, work in contact with CPAP helmets) and comorbidities (hypertension).

Secondly, we selected the subsample of HCWs who were found positive for SARS-CoV-2. For these HCWs, we also collected data on safety at the workplace and community as correct use of personal protective equipment (PPE) and workstation safety. Sick days, exposure to confirmed case, number of positive nasopharyngeal swabs and time length of negativization were also collected. In addition, we collected clinical data from electronic medical records referring to symptoms reported at the time of the nasopharyngeal swab: fever, cough, shortness of breath, sore throat, conjunctivitis, gastrointestinal (GI) symptoms, asthenia, ageusia, anosmia, headache or neurological symptoms.

HCWs protection protocols

During the pandemic, the Infections Committee issued a protocol aimed to design HCWs protection strategy, which is structured as follows: with regards to safety at the workplace, training courses on the correct use of PPE were mandatory for the involved personnel. The Hospital stocked Class 2/3 Filtering Face-Piece respirator, surgical masks, liquid-repellent gowns certified for biological risk, hair cap, overshoes, goggles/face shield for all the involved HCWs according to the WHO guidelines.[7] A continuous supply of the aforementioned PPE was then guaranteed to all HCWs during the study period.

All these data were retrospectively collected on June 2020 by trained medical management doctors.

The study has been approved by the Ethics Committee of the IRCCS Policlinico San Matteo and has followed the principles of the Declaration of Helsinki.

SARS-CoV-2 detection

Laboratory confirmation of the SARS COV-2 infection has been defined as positive real-time reverse transcriptase polymerase chain reaction from clinical nasal swabs, which have been analyzed by the Molecular Virology Unit of our Hospital according to the WHO guidelines and Corman et al. protocols.[8]

Statistical analysis

The characteristics of the HCWs were described using medians and interquartile ranges (IQR) for the quantitative variables and absolute/relative frequency values for the qualitative ones. Comparison between HCWs who were infected and HCWs who were not infected by COVID-19 was performed using non-parametric Mann–Whitney U test for quantitative variables and Chi-squared or Fisher exact test for categorical variables. COVID-19 cumulative incidence and 95% confidence intervals were estimated considering the whole population of San Matteo health care workers as well as considering only the workers who underwent at least a nasopharyngeal swab for SARS-CoV-2 RNA detention from 22 February to 8 May 2020 (screened HCWs). The sample of screened workers was used, then, to perform a Poisson regression and calculate specific COVID-19 incidence rate ratios (IRRs) and 95% confidence intervals considering potential risk factors of COVID-19 infection. Predictors included in the statistical model were age, length of service in the hospital, sex, job role, working environment, body mass index (BMI), hypertension, smoking habit and alcohol consumption.

Analyses were performed using STATA software package (2018, release 15.1; StataCorp, College Station, TX).

Results

Of the 4632 HCWs working in our Hospital on 22 February 2020, 66.6% were females and their median age was 45.4 years (IQR: 32.2–54.2). With regards to job role, 1525 (32.9%) were physicians, 1321 (28.5%) were nurses, 860 (18.6%) were health care assistants, while the remaining 926 (20.6%) were administrative staff members. The median length of service was 11 years (IQR: 2–22). As of 8 May 2020, the infection was eventually confirmed by at least one nasopharyngeal swab test in 164 HCWs out of the 1447 screened.

COVID-19 incidence and risk factors in the HCWs

The COVID-19 cumulative incidence in the San Matteo Hospital in the study period was 3.54 (95%CI: 3.04–4.13) per 100 HCWs, while the cumulative incidence among the screened HCWs can be estimated as 11.33 (95%CI: 9.72–13.21) per 100 HCWs.

The epidemiological, lifestyles characteristics and risk factors for SARS-CoV-2 infection among our Hospital screened HCWs are shown in Table 1. Comparison between 164 HCWs who were infected and 1283 HCWs who were not infected showed similar median age, length of service in the hospital and a similar distribution of job roles, while males were slightly more prevalent among infected HCWs (36.6 versus 29.6%, $P = 0.068$). The working environment was significantly associated to COVID-19 infection ($P < 0.0001$): among 465 HCWs working in a COVID-19 ward and providing direct assistance to confirmed COVID-19 patients, 97 resulted positive to at least a nasopharyngeal swab test during the study period (59.1% of the whole sample of infected), while 368 resulted negative to the nasopharyngeal swab tests (28.7% of the whole sample of not infected); differently, 60 infected (37%) worked in other clinical wards, potentially COVID-19 patients-free, w.r.t. 756 not infected (59.6%). Eventually, 7 (4.3%) infected and 150 (11.3%) not-infected HCWs worked in the Hospital without any contact with patients at all. Contact with CPAP helmets (which were present in some of the COVID-19 wards) was also significantly associated to COVID-19 infection (48.4% of the infected versus 16% of the not-infected, $P < 0.0001$). Median BMI was higher (24.4 versus 23.4, $P = 0.01$) among infected versus not-infected workers while hypertension was similarly distributed (9.8 versus 8.3%, $P = 0.538$). More than 60% of the infected and not-infected HCWs never smoked, but there was a higher proportion of former smokers (20.1 versus 11.0%) and a lower proportion of current smokers (11.1 versus 24.3%) among infected w.r.t not infected ($P < 0.0001$); alcohol consumption was similarly distributed, conversely ($P = 0.34$).

Table 2 reports the results of the Poisson multivariable regression analysis performed to assess factors associated with different rates of SARS-CoV-2 infection.

Holding all other variables in the model constant, working in a COVID ward (compared with working in other clinical wards, IRR: 2.81, 95%CI: 1.95–4.03), being a former smoker (compared with being a person who had never smoked, IRR: 1.83, 95%CI: 1.27–2.62) and having a higher BMI (IRR: 1.03, 95%CI: 1.00–1.06) were significantly associated with an increased rate of SARS-CoV-2 infection. Males had a higher rate of infection compared to females, but the result was borderline significant (IRR: 1.37 95%CI: 0.97–1.92).

Furthermore, being a current smoker, compared with being a person who had never smoked, was associated to a reduced rate of infection (IRR: 0.43, 95%CI: 0.23–0.80).

Characteristics of HCWs who were infected by SARS-Cov-19

There were no differences between the epidemiological and immunological profile or symptom frequency of infected HCWs working in a COVID-19 ward w.r.t those working in other clinical wards, as well as there were no differences comparing infected males and females HCWs ($P > 0.05$ for

Table 1 Epidemiological characteristics and risk factors for COVID-19 in the HCWs of the IRCCS Policlinico San Matteo who underwent a nasopharyngeal swab test for SARS-CoV-2 detention from 22 February 2020 to 8 May 2020

HCWs	*All (N = 1447)*	*COVID-19 cases (N = 164)*	*Not infected (N = 1283)*	**P*
Age (years)	45.0 (IQR 33.2–53.4)	46.3 (IQR 35.4–53.7)	44.9 (IQR 33.0–53.4)	0.427
Length of service (years)	11.3 (IQR 2.0–21.8)	11.4 (IQR 2.6–20.6)	11.3 (IQR 2.0–22.3)	0.918
Sex				
Men	440 (30.4%)	60 (36.6%)	380 (29.6%)	0.068
Women	1007 (69.6%)	104 (63.4%)	903 (70.4%)	
Job category				
Administrative staff	178 (12.3%)	13 (7.9%)	165 (12.9%)	0.24
Health care assistant	255 (17.6%)	34 (20.7%)	221 (17.2%)	
Nurse	568 (39.3%)	63 (38.4%)	505 (39.4%)	
Physician	446 (30.8%)	54 (32.9%)	392 (30.6%)	
Working environment				
COVID-19 ward	465 (32.1%)	97 (59.1%)	368 (28.7%)	<0.0001
Non-COVID-19 clinical ward	825 (57.0%)	60 (36.6%)	765 (59.6%)	
No contact with patients	157 (10.9%)	7 (4.3%)	150 (11.7%)	
Contact with CPAP helmets				
No	1169 (80.8%)	91 (55.2%)	1078 (84.0%)	<0.0001
Yes	278 (19.2%)	73 (44.8%)	205 (16.0%)	
BMI (kg/m^2)	23.4 (IQR 20.7–26.5)	24.4 (IQR 21.8–26.8)	23.4 (IQR 20.6–26.4)	0.012
Smoking habit				
Never	721 (65.2%)	113 (68.9%)	608 (64.5%)	<0.0001
Former	138 (12.5%)	33 (20.1%)	105 (11.1%)	
Current	247 (22.3%)	18 (11.0%)	229 (24.3%)	
Hypertension				
No	1064 (91.5%)	148 (90.2%)	916 (91.7%)	0.538
Yes	99 (8.5%)	16 (9.8%)	83 (8.3%)	
Alcohol consumption				
None	340 (32.0%)	34 (28.3%)	306 (32.5%)	0.340
Moderate	677 (63.7%)	83 (69.2%)	594 (63.1%)	
Not moderate	45 (4.2%)	3 (2.5%)	42 (4.5%)	
High	0 (0.0%)	0 (0.0%)	0 (0.0%)	

Notes: COVID-19 = coronavirus-19 disease; HCWs = health care workers; CPAP = continuous positive airway pressure

Data are absolute frequency (% in the group) or median value (interquartile range, IQR).

*We compared COVID-19 versus not-infected HCWs groups using Mann–Whitney U test for quantitative variables and Chi-squared test for qualitative ones. Statistical significance $P < 0.05$.

Missing data: among 1283 non-infected HCWs, BMI was available for 939, smoking for 942, hypertension for 999 and alcohol for 942, respectively; alcohol consumption information was available for 120 out of 164 COVID-19 cases.

all features). Therefore, Table 3 describes specific features and clinical characteristics of the whole sample of COVID-19-infected HCWs.

The majority of the infected individuals were symptomatic (90.2%) at the first place, and the most common symptom was the fever (69.5%), followed by asthenia (44.5%), ageusia (36%) and anosmia (40%).

On average, positive HCWs were absent from work for 18 days and the mean time to negativization of swab was 16 days. None of the HCWs died because of COVID-19 infection, and 5.5% had a hospital admission.

Discussion

Admittedly, as previous SARS-CoV-1 and Ebola Virus epidemics have taught us, the HCWs who are firstly involved in fighting highly infectious diseases are at a great risk of infection.[7–9]

Table 2 Multivariable Poisson regression for estimating the relative incidence rates of COVID-19 among screened HCWs, considering potential risk factors

HCWs characteristics	*Adjusted IRR(95%CI)*	*P*
Age (years)	1.02 (0.99–1.05)	0.137
Length of service (years)	0.98 (0.96–1.01)	0.175
Sex		
Men	1.37 (0.97–1.92)	0.076
Women	1	
Job category		
Administrative staff	1.24 (0.60–2.55)	0.556
Health care assistant	1.08 (0.64–1.83)	0.768
Nurse	1.49 (0.97–2.30)	0.070
Physician	1	
Working environment		
Without contact with patients	0.67 (0.30–1.48)	0.322
COVID ward	2.81 (1.95–4.03)	<0.0001
Other clinical ward	1	
BMI (kg/m^2)	1.03 (1.00–1.06)	0.031
Hypertension		
No	1	
Yes	1.01 (0.58–1.75)	0.968
Smoking habit		
Never	1	
Former	1.83 (1.27–2.62)	0.001
Current	0.43 (0.23–0.80)	0.008
Alcohol consumption		
None or moderate	1	
Not moderate	0.53 (0.17–1.64)	0.271

Notes: BMI=Body Mass Index

Sample size analyzed: 1022 HCWs with no-missing information for all variables considered. Adjusted IRR, 95% confidence intervals (95% CI) and *P* values (P) were obtained: (i)for the categorical variables comparing the different categories relative to the reference category indicated by IRR = 1; (ii)per one unit increase of the continuous variables.

The SARS-CoV-2 transmission through person-to-person contact and, consequently, also among HCWs, might result in a harmful shortage of medical staff, which fuels the concern of a collapse of the health care systems in the most hit regions worldwide.

The role of HCWs as 'heroes' and their best practice in a dramatic, pandemic context have been often enhanced by widespread media reports of fatigue and burnout.[12,13]

However, data on risk factors and clinical or lifestyle characteristics of infected HCWs are widely lacking and surveillance for new reports on this subject is ongoing.[14]

Since the non-aligned timing of COVID-19 pandemic worldwide, we believe that sharing our experience as a hard and early hit country has important implications for ensuring the protection of essential workers from the infection risks.

Among the screened HCWs of our Hospital, we found a cumulative incidence of SARS-CoV-2 infection of 11.33% (95%CI: 9.72–13.21). The disease was found to be mild in most cases, requiring hospitalization in only 5% of cases and, notably, nobody died. In addition, at the time of writing, no more new cases among HWs occurred.

To confirm our results, few Italian data have shown quite a high prevalence of COVID-19 infection among HCWs, which exceeds 5% of the total.[15,16] On 16 April 2020, the Italian National Institute of Health (ISS) reported that 16 991 (10.7%) HCWs had tested positive for SARS-CoV-2.[17] Notably, results from Southern Italy, where the spread of contagion was significantly lower, are quite different from ours reporting a prevalence of infection of only 0.4%.[18]

However, infection rates of HCWs are extremely variable worldwide. Reports from Spain, UK and the Netherlands[19–23] have detected an even higher prevalence while other data from Germany, China and United States have shown significantly lower numbers.[24–28]

Table 3 Epidemiological, immunological and clinical profile of COVID-19 infected HCWs

HCWs characteristics (N = 164)	
Exposure to confirmed COVID-19 cases	33 (20.1%)
Number of positive nasopharyngeal swabs	1.0 (IQR 1.0–1.0), range: 1–4
Sick days	18.0 (IQR 13.5–25.0)
Time length of negativization (days)	16.0 (IQR 12.0–20.0)
Clinical profile (N = 164)	
Hospital admission	9 (5.5%)
Presence of symptoms	148 (90.2%)
Fever (ABT > 37.5 °C)	114 (69.5%)
Asthenia	73 (44.5%)
Anosmia	67 (40.9%)
Ageusia	59 (36.0%)
Cough	59 (36.0%)
Neurological symptoms and headache	42 (25.6%)
GI symptoms (nausea and diarrhea)	35 (21.3%)
Dyspnea	34 (20.7%)
Sore throat	28 (17.1%)
Conjunctivitis	11 (6.7%)

Notes: COVID-19 = coronavirus-19 disease; HCWs = health care workers; PPE = personal protective equipment; ABT = axillary body temperature; GI = gastrointestinal.

Data are absolute frequency (% in the group) or median value (inter-quartile range, IQR).

In our research, the relative incidence rate of SARS-CoV-2 was higher between HCWs working in COVID-19-dedicated wards than HCWs working in other wards.

Among HCWs, occupational exposure to the virus is certainly of great concern. Specifically, due to the possibility of transmission by droplets, maneuvers like intubation, non-invasive ventilation and manipulation of oxygen masks or continuous positive arterial pressure (CPAP) helmets might be considered as potentially risky. Consequently, intensive care (IC) and first-aid personnel have often been regarded as the most exposed. In a similar manner, in the view of a large amount of SARS-CoV-2-hospitalized-infected patients in the infectious and respiratory diseases units, working in the aforementioned facilities has been assumed to be risky too. Accordingly, the prevalence of infection among the medical staff members in centers receiving COVID-19 patients has been reported as much higher than that of centers not receiving COVID-19 patients.[29] In the same way, physicians, nurses and health technicians with direct contact with COVID-19 patients have been more likely to be infected than those without, like clerical workers.[16] However, several studies have not identified a statistically significant difference in the proportion of infected HCWs from hospital units firstly involved in close contact with COVID-19 patients compared with intermediate- or low-risk units.[20,30,31]

At a first glance, we might be surprised that all these potentially hardest hit groups of HCWs have not been the most infected by the virus at the very end.

One might, however, observe that this finding is not that surprising, since PPE and other general protective measures have been initially unavailable in clinical departments other than first-line infectious and respiratory diseases units. Accordingly, non-first-line HCWs might have been exposed to a heightened risk of infection.

Notably, in our Hospital, the Infections Committee issued a protocol to all HCWs regarding the management of suspected or ascertained COVID-19 cases on 31 January 2020, before the first Italian case was confirmed. This helped estimating in advance the real urgency for PPE for all the staff, and not only for the most exposed wards. Furthermore, and perhaps most importantly, our Hospital immediately trained all the HCWs on the appropriate use of PPE. Over 1.200 HCWs attended several courses before and during the outbreak.

Consequently, we may safely agree that, assuming the equal accessibility and proper use of PPE of all the HCWs of our Hospital, the great and more prolonged contact with COVID-19 patients remained a crucial risk factor for SARS-CoV-2 infection among HCWs. This finding is indeed confirmed by the literature.[32,33]

The majority of the available studies have attributed a mild or moderate disease severity to the COVID-19 infected HCWs.[14,19,34–36] Moreover, although possibly under-reported, the case-fatality rate varies between countries and time of disease outbreak but remains quite low.[37,38]

Despite the well and sadly known high case fatality rate in our country,[39] and the warning of a worldwide echo in the early pandemic phases,[40] the sheer consistency of our results should come as no surprise to us.

Hence, severe illness and death predominantly occurs in elderly patients with underlying medical comorbidities, and conversely, affected HCWs are usually younger people with less predisposing conditions. Furthermore, early symptoms are more easily noticed by HCWs themselves and treatment urgently started.

Since several conditions have been associated with severe illness and mortality in the community,[41] HCWs' risk factors and medical comorbidities have not been uniformly reported in literature.[13,37,42] We have considered HCWs lifestyle and medical history of our Hospital staff. In our experience, being an active smoker is associated to a reduced rate of SARS-CoV-2 infection. However, the impact of current smoking on COVID-19 is controversial.[43,44] Our results are in line with those by Lippi et al.,[45] but we believe that this is an intriguing diatribe. Whether cessation of smoking indeed improves pulmonary function, it is as well known that this benefit is decreased by the cumulative injury of smoke to the lungs. Therefore, it is strongly associated with the smoking period of time. This figure, which indicates a complicated relationship between smoking history and the severity of COVID-19, often lacks in literature and further research is warranted.

We are aware of several limits of this study. Firstly, there are some missing data on all the tested HCWs. Specifically, clinical data are available only for the positive HCWs sample. Furthermore, due to the retrospective nature of this study, recall missing data results tricky.

Secondly, we have tested the HCWs only in presence of typical symptoms or unprotected contacts with COVID-19 patients. Indeed, in the eye of the storm, in our hardly hit Hospital at the beginning of the pandemic, nasal swabs for SARS-CoV-2 RNA detention in HCWs have been justified by epidemiological and clinical criteria. With the gift of hindsight, we currently know that this has been a weakness. However, the decisions of those days have been determined by the emergency circumstances, definitely unrivalled in the history of medical care, which have overwhelmed the health care system on all fronts and have not certainly ceased.

In the event of a regrettably increasingly plausible second wave of contagions, which seems we are now aware of the several, potential benefits of universal staff testing.[21] On the one hand, it would boost working staff depletion by identifying only the symptomatic HCWs who really have COVID-19 and avoiding the substantial proportion of faulty self-isolation of the others. On the other, it would undoubtedly limit the risk of asymptomatic spread of SARS-CoV-2.[15,16,30,46] Asymptomatic HCWs might become, indeed, a significant risk factor for patients, colleagues and the community.

Authors Contributions

All authors provided critical feedback and helped shape the research, analysis and manuscript. VN, AM, SC and GR conceived the original idea and, together with CM and MCM designed the experimental plan; MC took the lead in writing the manuscript, GR, VN, SC, CR, AMG and VZ contributed to sample preparation and revision of medical records collection; MCM and CR performed record linkage between data sources; GR and MCM took care of the quality control of the data and MCM performed the statistical analyses. AM and CM supervised the findings of this work. MC and CM contributed to the interpretation of the results. All authors participated to the revision of the final manuscript and approved it.

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Conflict of interests

None related to the content of this manuscript.

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