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REVIEW

Measles among healthcare workers in Italy: is it time to act?

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ABSTRACT

Vaccination of healthcare workers (HCWs) against measles is strongly recommended in Europe. In this study, we examined the impact of measles on Italian HCWs by systematically and quantitatively analyzing measles cases involving HCWs over time and by identifying the epidemiological characteristics of the respective measles outbreaks. We retrieved data on measles cases from the Italian national integrated measles and rubella surveillance system from January 2013 to May 2019. Additionally, we performed a systematic review of the literature and an analysis of the measles and rubella aggregate outbreaks reporting forms from 2014 to 2018. Our review suggests that preventing measles infection among HCWs in disease outbreaks may be crucial for the elimination of measles in Italy. National policies aiming to increase HCW immunization rates are fundamental to the protection of HCWs and patients, will limit the economic impact of outbreaks on the institutions affected and will help achieve the elimination goal.

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Measles; outbreaks; healthcare workers; Italy; review

Introduction

In recent years, a dramatic drop in measles vaccination coverage, which is likely responsible for multiple epidemic peaks, has been registered in Europe.[1,2] In 2017, Italy suffered one of the highest measles infection rates[3-5] and its Parliament approved an extraordinary ordinance (Italian Decree Law n. 73/2017) that extended the number of compulsory vaccinations for school admission and included vaccination against measles.[6] After the introduction of this law, official data indicate an increase in childhood immunization coverage.[7,8] Despite this encouraging progress, measles has continued to spread across the country. According to the Italian National Institute of Health (NIH), 1334 measles cases were registered in the first six months of 2019, more than 80% of which occurred in people aged between 15 and 64 years,[9] suggesting a significant vaccination gap among young people and adults in Italy.

In this context, growing attention has been paid to healthcare workers (HCWs): compared to the general population, HCWs are estimated to be at greater risk of acquiring vaccine preventable diseases such as measles, exposing both their colleagues and patients to contagion.[10,11] Measles can easily spread across nosocomial settings where a large number of contacts is possible:[11,12] measles infections may be associated with a high risk of poor outcomes for hospitalized patients[12,13] and can cause a huge economic impact on the healthcare centers affected.[14,15] Currently, although HCW vaccination against measles is strongly recommended in Italy,[16] in 2018 two Italian Regions, Emilia-Romagna and Puglia, were forced to introduce a regulatory restriction when hiring HCWs to check their immune status; where susceptible workers refuse vaccination, they are reallocated away from high-risk settings (i.e. Oncology, Hematology) to other wards.[17,18]

A few researchers have investigated the impact of measles on HCWs[10,19,20] or have assessed their immune status,[21-24] often yielding disturbing results. Thus, further research is needed to understand the extent of vaccine noncompliance among HCWs and to develop effective measures to combat this behavior. To the best of our knowledge, this is the first systematic analysis of the evidence on measles cases and HCWs. In particular, this study has two purposes: first, we aimed to investigate measles cases among HCWs and to quantify the issue over time; second, we wished to identify the epidemiological characteristics of the measles outbreaks involving HCWs to make available further information relevant to the public health debate on vaccination policies.

Methods

To provide a comprehensive picture of the phenomenon, multiple data sources were investigated. Thus, to analyze measles cases in HCWs, we retrieved data from the national integrated measles and rubella surveillance system, whereas to investigate the key features of measles outbreaks involving HCWs, we performed a systematic review of the literature and an analysis of the measles and rubella aggregate outbreaks reporting forms.

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Analysis of measles cases among HCWs

Since 1st January 2013, measles and rubella surveillance has been integrated in a unique surveillance system. All 19 Regions and the two Autonomous Provinces (APs) of Italy, hereafter collectively referred to as "Regions", participate in the scheme by reporting through an online platform. In this study, we analyzed the reported measles cases involving HCWs from database inception to 15th May 2019. For each case, additional data were retrieved: date and Region, HCW characteristics (gender, age, vaccination status), virus genotype, setting (hospital: emergency department or ward; community: family, school, other workplace, nomadic camp), case classification (confirmed, probable or possible) and type (sporadic: when it was not part of an outbreak; outbreak-associated: when a link with other cases was established). Case classification was based on the standard European Union case definition.[25]

Analysis of measles outbreaks involving HCWs

Systematic review of the literature

This review employs the methods outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.[26-28]

Selection criteria, search methods and study selection

We included any report that respected the following criteria: (i) describes one or more measles outbreaks; (ii) the outbreak/s occurred in Italy; (iii) at least one HCW was infected. A HCW was defined as a person engaged in actions whose primary intent is to improve the health of members of the public, and included students, nurses, physicians and other paramedical professional figures.[29] A measles outbreak was defined as two or more linked cases, either epidemiologically or by genotype. We excluded articles that described hospital measles outbreaks where none of the aforementioned personnel was infected. Reports in English or Italian were considered eligible. No time restriction was applied.

The review was performed by searching the bibliographic databases Pubmed, Scopus and ISI Web of Science. The search terms were grouped in the following string: (Epidem* OR Outbreak) AND measles AND Ital* AND (nosocom* OR healthcare OR health-care OR health care OR hospital*). The string was adapted to fit the search criteria of each database. The search was supplemented by exploring the web sites of the Regions for other reports describing measles outbreaks involving HCWs in Italy and by scanning the reference lists of all the relevant articles we retrieved.

Duplicate articles were removed, and the title and abstract of all retrieved records were screened. Studies that did not meet the inclusion criteria were excluded. Full texts of potentially relevant articles were examined by two researchers and reasons for exclusion were recorded. When outbreak reports were updated by other reports, only the most recent was analyzed. Disagreements were resolved by consensus or by a third reviewer.

Data collection and quality assessment

Articles were divided into two categories according to the description of the outbreaks. When the record described more than one outbreak simultaneously (i.e. multiple outbreaks), the following information was retrieved: first author and year of publication; start date and end date; geographic area where the outbreaks took place; number of infected HCWs out of the total number of confirmed cases; virus genotype. For articles investigating outbreaks separately (i.e. single outbreaks), the following data were collected for each of them: first author and year of publication; start date and end date of the measles outbreak; Region or Province involved; description of the index case; setting; number of infected HCWs out of the total number of cases (i.e. outbreak size); virus genotype. The outbreak setting was defined as "hospital" if it originated and/or spread within the healthcare environment; "community" if it originated and/or spread elsewhere and did not reach the healthcare environment; "hospital-community" if both settings were involved.

The quality assessment was performed using the ORION statement, a 22-item checklist for Outbreak Reports and Intervention Studies of Nosocomial infection.[30] Two reviewers independently assessed report quality and disagreements were resolved by consensus or by a third reviewer.

Measles and rubella aggregate outbreaks reporting forms

The measles and rubella aggregate outbreak reporting forms are part of the Annual Status Update, a national report which is submitted annually to the World Health Organization (WHO) Regional Office for Europe by the Italian National Verification Committee for Measles and Rubella Elimination. Each form relates to one outbreak and is made up of two parts: 1) data on outbreak identification, case detail and laboratory detail; 2) two boxes for the description of the main epidemiological findings of the outbreak and the control measures, respectively.[31] The forms for the five-year period 2014–2018 were retrieved and all the outbreaks involving at least one HCW were analyzed. The same criteria used to collect information on the single measles outbreaks retrieved from the systematic review were applied to each outbreak reporting form. For the outbreak size, it was deemed small if it involved from two to five people; medium if it involved from six to ten people; large if it involved more than ten people.

Results

Analysis of measles cases among HCWs

Among the measles cases which occurred in working-age people, there was considerable year-to-year variation in both the total number of cases and the proportion reported in HCWs: the national surveillance system registered 119 cases in HCWs out of a total of 1472 (8.1%) in 2013, 83/1066 (7.8%) in 2014, 2/148 (1.4%) in 2015, 66/459 (14.4%) in 2016, 334/3796 (8.8%) in 2017 and 126/1871 (6.7%) in 2018. Table 1 shows the characteristics of the measles cases notified as involving HCWs.

More than 65% of the total number of HCW measles cases occurred in six Regions (Lazio, Lombardia, Toscana, Sicilia, Emilia-Romagna and Piemonte), that are among the nine

Table 1. Characteristics of measles cases notified in Italy as involving healthcare workers (HCWs) in the national integrated measles and rubella surveillance system from 2013 to 2018.

	Total 2013–2018 N (%)	2013 N (%)	2014 N (%)	2015 N (%)	2016 N (%)	2017 N (%)	2018 N (%)
Region	730 (100)	119 (100)	83 (100)	2 (100)	66 (100)	334 (100)	126 (100)
Piemonte	57 (7.8)	16 (13.4)	5 (6.0)	0 (0.0)	7 (10.6)	29 (8.6)	0 (0.0)
Lombardia	88 (12.1)	50 (42.0)	3 (3.6)	2 (100)	9 (13.7)	20 (6.0)	4 (3.2)
AP Bolzano	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0)	0 (0.0)	1 (0.8)
AP Trento	4 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	2 (3.0)	2 (0.6)	0 (0.0)
Veneto	33 (4.5)	0 (0.0)	7 (8.5)	0 (0.0)	2 (3.0)	20 (6.0)	4 (3.1)
Friuli–VG	14 (1.9)	4 (3.4)	2 (2.4)	0 (0.0)	1 (1.6)	4 (1.2)	3 (2.4)
Liguria	31 (4.2)	11 (9.2)	6 (7.2)	0 (0.0)	0 (0)	4 (1.2)	10 (7.9)
Emilia-Romagna	57 (7.8)	14 (11.8)	22 (26.5)	0 (0.0)	12 (18.2)	4 (1.2)	5 (4.0)
Toscana	76 (10.4)	6 (5.0)	3 (3.6)	0 (0.0)	4 (6.1)	59 (17.7)	4 (3.2)
Marche	23 (3.2)	4 (3.4)	7 (8.5)	0 (0.0)	2 (3.0)	7 (2.1)	3 (2.4)
Lazio	162 (22.2)	0 (0.0)	8 (9.6)	0 (0.0)	8 (12.1)	128 (38.3)	18 (14.3)
Umbria	20 (2.7)	0 (0.0)	0 (0.0)	0 (0.0)	3 (4.5)	17 (5.1)	0 (0.0)
Abruzzo	26 (3.6)	13 (11.0)	2 (2.4)	0 (0.0)	0 (0.0)	4 (1.2)	7 (5.5)
Puglia	7 (1.0)	0 (0.0)	3 (3.6)	0 (0.0)	0 (0.0)	1 (0.3)	3 (2.4)
Basilicata	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
Calabria	13 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	5 (7.6)	5 (1.5)	3 (2.4)
Campania	33 (4.5)	0 (0.0)	1 (1.2)	0 (0.0)	6 (9.1)	5 (1.5)	21 (16.7)
Sicilia	63 (8.6)	0 (0.0)	0 (0.0)	0 (0.0)	2 (3.0)	22 (6.6)	39 (30.9)
Sardegna	21 (2.9)	1 (0.8)	14 (16.9)	0 (0.0)	3 (4.5)	2 (0.6)	1 (0.8)
HCW gender	730 (100)	119 (100)	83 (100)	2 (100)	66 (100)	334 (100)	126 (100)
Male	264 (36.2)	33 (27.7)	23 (27.7)	1 (50.0)	23 (34.8)	122 (36.5)	62 (49.2)
Female	466 (63.8)	86 (72.3)	60 (72.3)	1 (50.0)	43 (65.2)	212 (63.5)	64 (50.8)
HCW age	730 (100)	119 (100)	83 (100)	2 (100)	66 (100)	334 (100)	126 (100)
18–39 years	522 (71.5)	90 (75.6)	56 (67.5)	2 (100)	47 (71.2)	241 (72.2)	86 (68.2)
> 39 years	208 (28.5)	29 (24.4)	27 (32.5)	0 (0.0)	19 (28.8)	93 (27.8)	40 (31.8)
HCW vaccination status	676 (100)	113 (100)	76 (100)	2 (100)	64 (100)	306 (100)	115 (100)
Unvaccinated	610 (90.2)	112 (99.1)	68 (89.5)	2 (100)	59 (92.2)	265 (86.6)	104 (90.4)
Vaccinated							
One dose	48 (7.1)	1 (0.9)	8 (10.5)	0 (0.0)	4 (6.3)	27 (8.8)	8 (7.0)
Two doses	12 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.5)	8 (2.6)	3 (2.6)
Unknown n. of doses	6 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	6 (2.0)	0 (0.0)
Measles genotype	203 (100)	20 (100)	11 (100)	1 (100)	30 (100)	99 (100)	42 (100)
B2	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.4)
B3	134 (66.0)	0 (0.0)	9 (81.8)	1 (100)	21 (70.0)	68 (68.7)	35 (83.3)
D4	2 (1.0)	2 (10.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
D8	64 (31.5)	17 (85.0)	2 (18.2)	0 (0.0)	8 (26.7)	31 (31.3)	6 (14.3)
D9	1 (0.5)	1 (5.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
H1	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (3.3)	0 (0.0)	0 (0.0)
Setting of infection	213 (100)	18 (100)	30 (100)	1 (100)	22 (100)	88 (100)	54 (100)
Hospital							
ED	19 (8.9)	4 (22.3)	3 (10.0)	0 (0.0)	0 (0.0)	4 (4.6)	8 (14.8)
Ward	179 (84.0)	12 (66.7)	25 (83.4)	1 (100)	21 (95.5)	80 (90.8)	40 (74.1)
Community							
Family	12 (5.6)	1 (5.5)	1 (3.3)	0 (0.0)	1 (4.5)	4 (4.6)	5 (9.3)
School	1 (0.5)	1 (5.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Workplace	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)
Nomadic camp	1 (0.5)	0 (0.0)	1 (3.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Case classification	730 (100)	119 (100)	83 (100)	2 (100)	66 (100)	334 (100)	126 (100)
Confirmed	636 (87.1)	101 (84.9)	70 (84.3)	2 (100)	57 (86.4)	302 (90.4)	104 (82.5)
Probable	44 (6.0)	10 (8.4)	8 (9.7)	0 (0.0)	6 (9.1)	15 (4.5)	5 (4.0)
Possible	50 (6.9)	8 (6.7)	5 (6.0)	0 (0.0)	3 (4.5)	17 (5.1)	17 (13.5)
Case type	658 (100)	97 (100)	74 (100)	2 (100)	62 (100)	305 (100)	118 (100)
Sporadic	365 (55.5)	69 (71.1)	34 (46.0)	1 (50.0)	19 (30.6)	182 (59.7)	60 (50.8)
Outbreak-associated	293 (44.5)	28 (28.9)	40 (54.0)	1 (50.0)	43 (69.4)	123 (40.3)	58 (49.2)
Number of outbreaks	157	13	21	1	25	61	36

AP: Autonomous Province; VG: Venezia Giulia; ED: Emergency Department.

most heavily populated Italian Regions and are also the six Regions where approximately 70% of the total number of measles cases occurred between 2013 and 2018 (data not shown). Only Molise and Valle d'Aosta reported no involvement of HCWs over the study period.

There were approximately twice as many female as male HCWs with measles across all years, with the exception of 2015 and 2018 when the two groups were similarly represented. Almost 70% of the infected HCWs were 18–39 years old and, of the 676 HCWs whose information on vaccination status was available, 90% were unvaccinated, a small percentage (7.1%) had received only one dose of vaccine, and smaller proportions had two doses or unknown doses of vaccine.

Virus genotype was reported in only 203 HCW cases, with B3 being the variant most frequently identified (66.0%). B3 started to circulate in 2014 and it was consistently found in more than 65% of HCW cases in subsequent years. In contrast, D8 was isolated in 64 HCWs (31.5% of the total genotyped cases); it represented the most frequent variant in 2013 and decreased in following years. The remaining genotypes were isolated in only one or two cases each throughout the study period.

The vast majority of infections were contracted in hospitals in each year considered. Overall, 8.9% of cases became infected in Emergency Departments and 84% in other wards. A small percentage of HCWs (5.6%) were infected by a relative. The remaining settings were responsible for only a single case each.

Most cases were reported as confirmed (87.1%), while probable or possible cases accounted for 6% and 6.9%, respectively. In general, sporadic cases were more frequently reported than outbreak-associated cases (55.5% *vs* 44.5%); nevertheless, in 2014 and 2016 most HCW cases were involved in measles epidemics and in 2015 and 2018 the two proportions (sporadic *vs* outbreak-associated) were similar. Lastly, the total number of outbreaks that involved HCWs over the study period was 157, ranging from a minimum of one in 2015 and a maximum of 61 in 2017.

Between 1st January and 15th May 2019, according to the surveillance system, 54/775 (7.0%) of notified measles cases among people of working age occurred in HCWs (data not shown), mainly in Lombardia and Lazio (20 and 15, respectively). Mostly, these HCWs were female (63%), aged between 18 and 39 years (81.5%), and unvaccinated (86%). More than 65% of the infections took place in hospitals. Twenty-seven cases were sporadic and 17 were outbreak-associated.

Analysis of measles outbreaks involving HCWs

Systematic review of the literature

Study selection. After removal of duplicates, 132 records resulted from the initial search (Figure 1). Screening by title and abstract selected 96 articles eligible for full text analysis, from which 84 records were excluded either because the measles outbreak(s) did not involve HCW infection (n = 61) or because the measles outbreak(s) did not occur in Italy (n = 23). Seven records were added to the previous 12 from the reference lists of relevant articles retrieved. Finally, a total of 19 records were included in this systematic review. Of the 19 articles included in this systematic review, six referred to multiple outbreaks,[32-37] while 13 described single outbreaks.[38-50]

Quality assessment. The ORION checklist was used to evaluate the quality of the 19 reports. Sixteen items of the ORION statement were considered applicable.

Considering the articles dealing with one outbreak, the majority of the items provided by the ORION statement were followed by each study, with the exception of the setting (adequately described in only 53.8% of the outbreaks) and the outbreak-related costs (never analyzed).

Considering the articles dealing with multiple measles outbreaks, the majority of the items provided by the ORION statement were followed by each study, with the exception of the control measures (reported in only three reports) and the economic impact (never investigated).

Characteristics of measles outbreaks. The data in the reports on multiple outbreaks were heterogeneous (Table 2). Two articles referred to a single city (Bologna and Milano) and another two referred to a particular Italian Region (Lazio and Emilia-Romagna), while the final two reports covered outbreaks that occurred throughout the country. The period analyzed in the reports ranged from a minimum of four months to a maximum of 15 months, and the size of the outbreaks varied from 26 to 5568 cases. The proportion of infected HCWs varied markedly between studies, with the highest percentages reported by Emilia-Romagna in 2016 (20.8%) and Milano (Lombardia) in 2017 (4.9%). Regarding virus genotype, B3 was the most represented, while D4 disappeared after 2010–2011, and D8 began to circulate in 2009–2010.

Of the 13 articles describing single outbreaks, two referred to the same outbreak, while one article reported two separate outbreaks, giving a total of 13 single measles outbreaks (Table 3). The Regions reporting the highest number of single outbreaks were Puglia and Emilia Romagna (n = 3), followed by Toscana (n = 2), while only one outbreak was described by AP Bolzano, Lombardia, Marche, Sicilia and Sardegna. The outbreaks occurred between 2006 and 2018, with 2017 being the most represented year. The index case was identified in 12 outbreaks: ten (83.3%) derived from patients admitted to hospital for measles-related symptoms who were not promptly diagnosed and isolated, while in two outbreaks (16.7%) the index cases were HCWs. All outbreaks (100%) reached the hospital setting and in nine outbreaks (69.2%) the community was also involved. The outbreak size was mostly large, with eight outbreaks (61.5%) involving more than ten people; two outbreaks (15.4%) were categorized as medium, while the remaining three (23.1%) were small. The number of infected HCWs was available in eleven cases; in three outbreaks (27.3%) only one HCW was implicated, in one case (9.1%) two HCWs were infected and in the other outbreaks (63.6%) more than three HCWs were involved. When available, the proportion of HCWs infected out of the total number of cases ranged from 1/17 to 4/5. Regarding the genotype, in 2006 only D4 was reported, whereas B3 was the most frequently recorded after 2014.

Measles and rubella aggregate outbreak reporting forms. From 2014 to 2018, 64 measles and rubella outbreak reporting forms detailed epidemiological features of the outbreaks involving HCWs. In particular, we found descriptions of 52.4% (11/21) of the outbreaks that occurred in 2014, 100% (1/1) of the outbreaks in 2015, 52% (13/25) of the outbreaks in 2016, 36.1% (22/61) of the outbreaks in 2017, and 47.2% (17/36) of the outbreaks in 2018. The main characteristics of such outbreaks are illustrated in Table 4.

Most outbreaks occurred in only one Region, apart from one case that was reported as having spread across two Regions in 2016. In general, the outbreaks were mainly notified by Toscana and Emilia-Romagna.

The index case was identified in 54 outbreaks: 19 outbreaks (35.2%) originated from patients admitted to hospital for measles-related symptoms, 18 index cases (33.3%) were HCWs, twelve (22.2%) were hospitalized patients, four (4.4%) were defined as hospital visitors (i.e. patients' relatives, outpatients) and in one case (1.8%) the infection started from someone outside the hospital who had contact with the HCW. Interestingly, the identification of patients admitted to hospital as the source of infection showed a gradual increase over

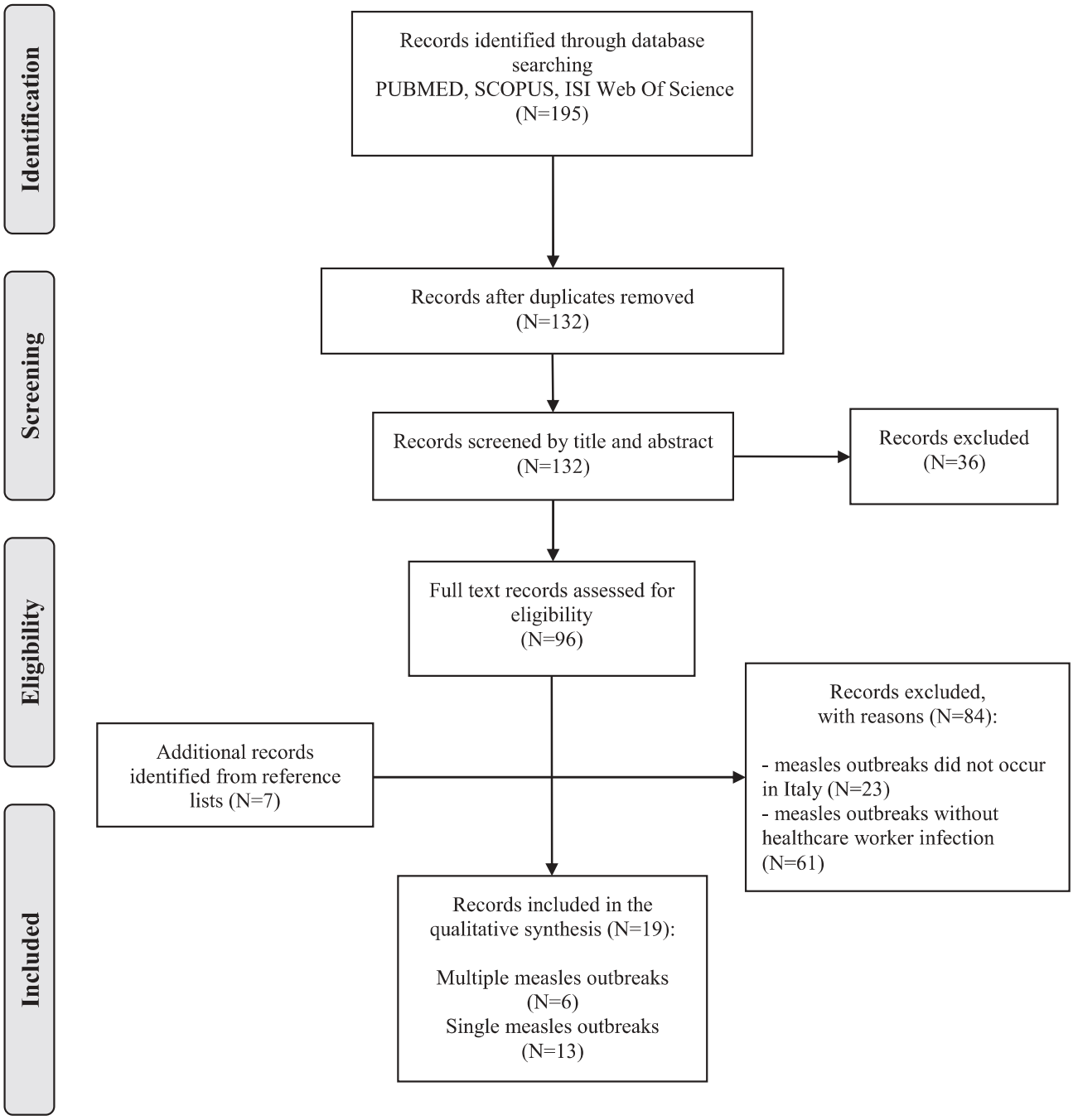

Figure 1. PRISMA flow diagram of the review process.

the study period, whereas the reporting of HCWs as index cases peaked in 2017. No further information on the role of HCWs in amplifying the measles outbreaks was available.

Most outbreaks remained confined to people working in or attending hospitals (46.9%) or occurred in both hospital and community settings (36.0%), while only 11 outbreaks (17.2%) occurred only in the community and in these cases, even if HCWs were infected, the outbreaks did not spread to hospitals. Overall, almost 80% of the outbreaks were of small size and this category was nearly always the most predominant in each individual year. By contrast, outbreaks of medium and large size occurred only between 2016 and 2018. In general, the number of infected HCWs was only one in 35 cases, while 24 outbreaks (37.5%) involved from two to three HCWs and, lastly, five outbreaks (7.8%) included more than three HCWs. Notably, while outbreaks with a low number of infected HCWs occurred throughout the study period, outbreaks with more than three HCWs were only reported in the last years.

Discussion

HCWs are a trusted source of information on vaccine safety and efficacy, and even though they should be highly

Table 2. Characteristics of multiple measles outbreaks occurring in Italy and involving at least one healthcare worker (HCW) included in the systematic review.

Author, year of publication	Year (duration)	Geographical area (City, Region or Region)	Number of infected HCWs/total number of confirmed cases (%)	Measles genotype
Calza, 2009	2007–2008 (6 months)	Bologna, Emilia-Romagna	1/26 (3.8)	not reported
Amendola, 2017	2017 (4 months)	Milano, Lombardia	10/203 (4.9)	D8, B3
Curtale, 2010	2006–2007 (15 months)	Lazio	4/449 (0.9)	D4, B3
Piccirilli, 2017	2016 (12 months)	Emilia-Romagna	15/72 (20.8)	B3, D8
Filia, 2011	2009–2010 (15 months)	15/21 Italian Regions and Autonomous Provinces	34/2151 (1.6)	D4, D8, B3
Filia, 2013	2010–2011 (15 months)	20/21 Italian Regions and Autonomous Provinces	185/5568 (3.3)	D4, D8, B3, D9, H1, A

Table 3. Characteristics of single measles outbreaks occurring in Italy and involving at least one healthcare worker (HCW) included in the systematic review.

Author, year of publication	Year (duration of the outbreak)	Region or Province	Index case	Setting	Number of infected HCWs/total number of cases	Measles genotype
Boncompagni, 2006 Bonanni, 2007	2006 (5 months)	Toscana	patient*	H, C	8/40	D4
Filia, 2007	2006 (3 months)	AP Bolzano	patient*	H, C	1/17	D4
Filia, 2008	2007 (n.s.)	Emilia-Romagna	patient*	H	3/4	not reported
Tafuri, 2009	2008 (1 month)	Puglia	patient*	H	1/2	not reported
Barbadoro, 2012	2011 (2 months)	Marche	patient*	H	4/5	not reported
Filia, 2015	2014 (6 months)	Sardegna	patient*	H	15/80	B3
Cozza, 2014	2014 (4 months)	Puglia	patient*	H, C	n.s./32	B3
Filia, 2016	2016 (4 months)	Emilia-Romagna	patient*	H, C	7/17	B3.1
	2016 (2 months)	Emilia-Romagna	HCW	H, C	5/7	B3.1
Rovida, 2018	2017 (2 months)	Lombardia	patient*	H, C	n.s./16	H1
Palamara, 2017	2017 (7 months)	Sicilia	unknown	H, C	2/57	B3
Porretta, 2017	2017 (3 months)	Toscana	HCW	H, C	15/35	B3.1
Martinelli, 2018	2018 (2 months)	Puglia	patient*	H, C	1/8	not reported

* Patient admitted to hospital.
H: Hospital; C: Community; AP: Autonomous Province; n.s.: not specified.

motivated to protect patients and society,[20] low vaccination coverages have led to a significant proportion of HCWs becoming infected during the current epidemic peaks.[20,51] Our study represents a systematic analysis of measles cases among Italian HCWs.

According to the national surveillance system, approximately 7% of measles cases occurring in working-age people still involve HCWs. Most of these are unvaccinated subjects aged between 18 and 39, suggesting that vaccination coverage is still low in younger adults and, given their consistent involvement in measles outbreaks, HCWs may be critical for the elimination process. Overall, the rate of laboratory investigations, with approximately 13% of HCW measles cases not confirmed, was quite satisfactory. Additionally, considering that the significant number of cases classified as sporadic was probably due to ineffective identification of the transmission chain and that the majority of HCWs contracted the virus in a hospital setting, it means that the percentage of measles cases linked to HCW infection may rise significantly when we take into account not only the HCWs, but also patients and hospital visitors. It is well-known that the healthcare setting carries a high risk of viral transmission[52] and that vaccination is the only reliable protection against nosocomial spread of measles;[53] for these reasons, the adoption of more stringent HCW vaccination policies at national level could represent a key measure for directly protecting HCWs themselves, indirectly protecting their patients and limiting the spread of any outbreak.

Although the systematic review found 19 reports of good quality, some methodological limitations should be outlined: (i) a detailed description of the settings was lacking in almost half of the single outbreak reports; (ii) the control measures were omitted in some cases; (iii) the economic impact of the outbreaks was not mentioned in any report.

In spite of the heterogeneous nature of the data, we witnessed an increasing reporting of HCWs' susceptibility to measles. Only three Regions published articles that described multiple measles outbreaks involving HCWs, half of them in the last three years. Moreover, the highest proportions of infected HCWs were reported in 2016 and 2017, which, given the higher measles incidence rate of the last years, could confirm the presence of an important vaccination gap in this group.

Similar considerations could be applied to single measles outbreaks, which were described by only few Regions. Since patients seeking care at the Emergency Department were the main source of infection, it is crucial for all HCWs to immediately recognize the prodromal phase of the infection and promptly isolate such individuals to avoid severe complications for susceptible patients.[54,55] No less importantly, HCWs may transmit measles to susceptible coworkers and family members, as happened in the reported outbreaks. It is fundamental to remember that, when more than one HCW is involved, the delivery of healthcare services may be compromised and the institutions involved can suffer additional costs due to the need for implementation of emergency measures.[55] In particular, nosocomial outbreaks of measles are associated

Table 4. Characteristics of measles outbreaks occurring in Italy and involving at least one healthcare worker (HCW) retrieved from the measles and rubella aggregate outbreak reporting forms from 2014 to 2018.

	Total N (%)	2014 N (%)	2015 N (%)	2016 N (%)	2017 N (%)	2018 N (%)
*Region (65)**	65* (100)	11 (100)	1 (100)	14* (100)	22 (100)	17 (100)
Piemonte	1 (1.5)	0 (0.0)	0 (0.0)	1 (7.1)	0 (0.0)	0 (0.0)
Lombardia	6 (9.2)	0 (0.0)	1 (100)	0 (0.0)	0 (0.0)	5 (29.3)
AP Trento	1 (1.5)	0 (0.0)	0 (0.0)	1 (7.1)	0 (0.0)	0 (0.0)
Veneto	3 (4.6)	0 (0.0)	0 (0.0)	1 (7.1)	0 (0.0)	2 (11.8)
Friuli–Venezia Giulia	2 (3.1)	0 (0.0)	0 (0.0)	1 (7.1)	0 (0.0)	1 (5.9)
Liguria	1 (1.5)	1 (9.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Emilia-Romagna	17 (26.2)	7 (63.6)	0 (0.0)	4 (28.7)	3 (13.6)	3 (17.6)
Toscana	18 (27.7)	1 (9.1)	0 (0.0)	2 (14.3)	13 (59.1)	2 (11.8)
Lazio	5 (7.7)	1 (9.1)	0 (0.0)	3 (21.5)	0 (0.0)	1 (5.9)
Abruzzo	2 (3.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (11.8)
Puglia	2 (3.1)	1 (9.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (5.9)
Sicilia	4 (6.2)	0 (0.0)	0 (0.0)	0 (0.0)	4 (18.2)	0 (0.0)
Sardegna	3 (4.6)	0 (0.0)	0 (0.0)	1 (7.1)	2 (9.1)	0 (0.0)
*Index case (54)***	54 (100)	6 (100)	1 (100)	11 (100)	20 (100)	16 (100)
Patient admitted to hospital	19 (35.2)	1 (16.7)	0 (0.0)	5 (45.5)	5 (25.0)	8 (50.0)
HCW	18 (33.3)	0 (0.0)	1 (100)	3 (27.3)	10 (50.0)	4 (25.0)
Hospitalized patient	12 (22.2)	5 (83.3)	0 (0.0)	2 (18.2)	2 (10.0)	3 (18.8)
Hospital visitor	4 (7.4)	0 (0.0)	0 (0.0)	0 (0.0)	3 (15.0)	1 (6.2)
People living in the community	1 (1.9)	0 (0.0)	0 (0.0)	1 (9.0)	0 (0.0)	0 (0.0)
*Setting (64)***	64 (100)	11 (100)	1 (100)	13 (100)	22 (100)	17 (100)
Hospital-community	23 (35.9)	3 (27.3)	0 (0.0)	6 (46.1)	6 (27.3)	8 (47.0)
Hospital	30 (46.9)	7 (63.6)	1 (100)	5 (38.5)	10 (45.4)	7 (41.2)
Community	11 (17.2)	1 (9.1)	0 (0.0)	2 (15.4)	6 (27.3)	2 (11.8)
*Outbreak size (64)***	64 (100)	11 (100)	1 (100)	13 (100)	22 (100)	17 (100)
Small	51 (79.7)	11 (100)	1 (100)	10 (76.9)	17 (77.3)	12 (70.6)
Medium	9 (14.1)	0 (0.0)	0 (0.0)	2 (15.4)	3 (13.6)	4 (23.5)
Large	4 (6.2)	0 (0.0)	0 (0.0)	1 (7.7)	2 (9.1)	1 (5.9)
*Number of infected HCWs (64)***	64 (100)	11 (100)	1 (100)	13 (100)	22 (100)	17 (100)
1	35 (54.7)	4 (36.4)	1 (100)	6 (46.2)	14 (63.6)	10 (58.8)
2–3	24 (37.5)	7 (63.6)	0 (0.0)	6 (46.2)	5 (22.8)	6 (35.3)
>3	5 (7.8)	0 (0.0)	0 (0.0)	1 (7.6)	3 (13.6)	1 (5.9)

* Number of outbreaks considering that one outbreak was notified by two Regions.
** Number of outbreaks with data available.

with absenteeism of susceptible HCWs after exposure, disruption of healthcare services and significant costs resulting from containment efforts.[56] On these grounds, the education and training of HCWs to allow them to promote and perform missing vaccinations after pre-vaccination screening could represent a cost-effective measure that would protect patients and HCWs, and would minimize the economic impact.[15,57]

Regarding reporting of measles genotype, the results are consistent with the trends described by the Measles and Rubella National Reference Laboratory of the Italian NIH: B3 and D8 co-circulated from 2014 to 2018, while D4 disappeared after 2014.[58,59]

Despite some improvements in the measles and rubella aggregate reporting forms,[60] a non-uniform degree of completeness of reporting was observed. It may not be a coincidence that the Regions that largely described the outbreaks were Toscana and Emilia-Romagna, which are ranked as well-performing Regions in the Measles Surveillance System.[60] The WHO states that measles surveillance data should guide the decision-making process in disease elimination programs.[61] Accurate investigations and subsequent reporting are fundamental to an understanding of transmission patterns and for monitoring measles outbreaks, thereby contributing to the identification of barriers and leading to appropriate adjustment of immunization strategies. In this context, our study suggests that outbreak reporting should be further improved to enhance the definition of plans for successful measles control.

To summarize, using multiple data sources highlighted different key aspects of the impact of measles on Italian HCWs. For example, most HCWs contracted the infection in a hospital setting, and hospitals were also involved in the majority of outbreaks. This is a crucial point to consider in terms of either morbidity and mortality of the patients or the economic impact on the institutions concerned. Second, although some Regions were more affected than others, our data show that HCW measles cases persist nationwide. Therefore, it may now be time to circumvent the regional fragmentation of the regulatory framework on vaccination policies by acting at the national level.[62] Last but not least, given that the vast majority of HCWs were aged between 18 and 39, our data suggest that a consistent vaccination gap may still exist in young adults.[1]

This study has some strengths and limitations. The main strength is the comprehensive collection and analysis of the available evidence on measles infections among HCWs. To the best of our knowledge, this is also the first attempt to both investigate HCW measles cases and systematically describe the main characteristics of the outbreaks in which they were involved. This combination of aspects provides a comprehensive picture of the phenomenon of HCWs' susceptibility to measles in the last years. We anticipate, therefore, that this study will attract the attention of decision makers at both the national and international levels.

By contrast, the major limitations are represented by the lack of accuracy of some data sources. Unfortunately, we are aware that the Italian Regions may have only partially and

inconsistently recorded measles cases among HCWs in the national surveillance system, probably resulting in under-reporting. Nevertheless, this bias may have been constant over the study period and, if it were corrected, it would only reinforce the demand for improvements in HCW vaccination programs. Moreover, a proportion of the outbreaks involving HCWs were not properly described in the measles and rubella outbreak reporting forms, and therefore they were impossible to synthesize. In particular, there is still a huge disparity across the Italian Regions in the quality of epidemiological reporting. Since this affected the availability of data, partly limiting the generalizability of the epidemiological features we found, the strengthening of the surveillance reporting system is essential for the monitoring of measles eradication and for the characterization of other localized populations with low vaccination coverage.

Conclusion

In spite of the remarkable progress made over the last two years, our data are consistent in showing that the measles elimination program in Italy is far from being completed and transmission of the measles virus in healthcare settings is still significant. Beyond serious morbidity and mortality, nosocomial outbreaks of measles are costly and disrupt the quality and safety of healthcare services. Since HCWs play a critical role in nosocomial transmission, the implementation of vaccination policies that aim to increase the HCWs' immunization rate is of the utmost importance in preventing the infection of both HCWs and patients, in limiting the economic impact of outbreaks on the institutions affected, and in finally achieving measles elimination in Italy.

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