

Healthcare workers' vaccination at European and Italian level: a narrative review

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Summary. Today some vaccine-preventable diseases remain an important cause of morbidity and mortality worldwide despite the availability of new vaccines. Healthcare workers are particularly at risk to acquire an infection disease, playing a fundamental role in nosocomial transmission, which makes them an important target group for vaccination. The vaccination recommendations of HCWs, as well as the general population, differ from country to country. Furthermore, coverage rates vary widely a lot over the world, making HCWs vulnerable to disease and so healthcare settings to outbreaks. The motivations of vaccine hesitancy are many and maybe other studies would help policymakers and stake-holders to shape programs to improve vaccination coverage and the control of infectious diseases through the correct application of guidelines on prevention. (www.actabiomedica.it)

Key words: healthcare workers, vaccination, coverage

Introduction

Healthcare workers (HCWs) were frequently implicated as the source of nosocomial infection by vaccine preventable diseases (VPDs) in health care settings. World Health Organization (WHO) estimates that all over the world about 59 million HCWs are potentially exposed every day to multiple occupational biological hazards, working with infectious patients and contaminated fluids and materials (1).

In hospital setting HCWs had frequent contact with high risk patients and they could lead to potential lethal infectious diseases and also, they could infect their colleagues (2,3).

So, the benefits of vaccinations of HCWs were many: they reduced the risk of outbreaks in health care facilities, decreased staff illness and absenteeism and also reduced costs resulting from loss of productivity (4-7).

Vaccines recommended for HCWs were summarized in Table 1.

In the 2017- 18 influenza season, 29 of European Member States recommended vaccination for HCWs: particularly, 23 of them reported that influenza immunisation was recommended for all HCWs; in Belgium, Norway, Portugal, Slovakia and Sweden flu was recommended for some HCWs (e.g. those working in out-patient, in-patient and long-term care departments). Also, within the United Kingdom vaccine recommendations varied: in Scotland vaccination was recommended for all HCWs, in England, Northern Ireland and Wales only for frontline or HCWs that have direct contact with patients. Although there is no national recommendation to vaccinate HCWs in Denmark, most regions and municipalities offer vaccinations to HCWs free of charge. In Sweden, vaccination was only recommended for staff caring for severely immunocompromised persons. In Slovakia, vaccination was recommended for HCWs in close contact with patients or the foci of infection. In all Member States that responded, the vaccination of HCWs is voluntary (8).

Table 1. Vaccines recommended for HCWs

Disease	Vaccination recommendations
Influenza	Recommended for all HCWs in the Europe, the USA and Japan. In Italy is mandatory for HCWs in Apulia, Emilia Romagna and Marche for all operative units.
Hepatitis B	Recommended for all HCWs in high-income countries. Mandatory for medical students in France. In Italy is mandatory for HCWs in Apulia, Emilia Romagna and Marche for all operative units.
Tetanus, diphtheria and pertussis	Recommended for all HCWs in high-income countries. Pertussis, in Italy is mandatory for HCWs in Apulia, Emilia Romagna and Marche for all operative units.
Measles, mumps and rubella	Recommended for all HCWs in high-income countries. Measles is mandatory in Finland and for female workers in Slovenia. In Italy is mandatory for HCWs in Apulia, Emilia Romagna and Marche for some operative units.
Varicella	Recommended for some or all HCWs in European countries

Also, almost all (29 of 30) European countries have established recommendations or requirements for hepatitis B vaccination, but with difference across Europe (9).

For tuberculosis (not here discussed) national recommendations regarding the immunization of health-care workers differ throughout Europe; a recent review evaluated the different recommendations in European countries: in four countries, BCG is required or recommended for all previously unvaccinated Mantoux-negative HCWs that may have contact with patients. In five other countries, immunization is only recommended for HCWs who are employed in high-risk sectors. In one country, the recommendations vary according to the HCWs' age. Finally, 4 countries do not currently recommend immunization against TB for HCWs (10). In France since April 2019, the BCG vaccination requirement not exists for healthcare workers and the social sector (11). Vaccination guidelines against tetanus, diphtheria, and pertussis varied across the countries but generally it is administered every 10 years with some exceptions (12,13).

MMR immunization is mandatory for HCWs in Finland for female workers in Slovenia and voluntary for all or specific groups of HCWs in 18 European countries; no immunization policies for HCWs against measles are in place in the remaining 11 European countries (14).

For CDC the following vaccinations was recommended for HCWS: hepatitis b, flu, MMR for born in 1957 or later not naturally or artificial immunized,

Tdap, chickenpox and those who are routinely exposed to isolates of *N. meningitidis* should get one dose of meningococcal vaccine (15).

Despite the above mentioned issues, several Authors have reported suboptimal immunization rates for some relevant VPDs among HCWs in most of countries, including Italy; even with professionals at high-risk of exposure to hazardous biological agents, such as those employed in obstetric or neonatology departments, this issue is important taking into account the evidence of nosocomial transmission, as reported in recent reports (16-22).

Below, we report the findings of a narrative review of the literature for some VPDs (i.e., HBV, measles, rubella, chickenpox and influenza) carried out in order to update the socio-demographic and professional characteristics, the susceptibility and the vaccination rates among HCWs in the world.

Hepatitis B

This is a vaccine preventable disease but despite this, today approximately 360 million carriers were present worldwide (23). HCWs are at particularly high risk, primarily due to their increased risk of exposure to blood (24).

The prevalence of chronic HBV varies widely around the world and WHO estimates that in 2015, 3.5% of the population were living with chronic HBV infection in the world. The African and Western Pacific regions accounted for 68% of those infected. In

2015, global coverage with the third dose of hepatitis B vaccine reached 84%, but the European, Eastern Mediterranean and African regions faced coverage gaps (25).

Benefits and risk in healthcare settings

Approximately 3 million healthcare workers per year receive an injury with an occupational instrument, with around 2,000,000 HCWs exposures to hepatitis B virus; today the rates of HBsAg positivity in healthcare workers reported in several studies published in the last three decades range from 0.1% to 8.1% (26-28). Low rates of HBsAg positivity were found in two seroprevalence studies conducted on healthcare workers in the United States (0.1%) and Brazil (0.8%)(29).

So, a cycle of vaccination is required for HCWs; if there isn't any serological response (HbsAB < 10 UI/ml) HCWs should repeat the 3-dose series and test for anti-HBs 1-2 months after the last dose of vaccine. If the HCW is still negative after the second vaccine series, the HCW is considered a non-responder to hepatitis B vaccination. It is also possible that the non-responder is chronically infected with HBV. HBsAg testing can be offered or suggested to determine if this is the case (30). Also Hepatitis B immunoglobulins were necessary if the HCWs are exposed to a unknown source or serological positive within 48 hours (31).

Vaccination coverage

Notwithstanding these recommendations, vaccination coverage against HBV remains suboptimal, albeit higher than with other recommended vaccines. For example, in a recent multicentre study in Italy, vaccination coverage was 77.3% for HBV (26). Vaccination coverage of HCWs against HBV in the USA was 63.4% and higher in French healthcare students (91.8%), probably for mandatory vaccination (20,32-34). In a study in China 86% of respondents reported having received at least one dose of the hepatitis B vaccination and 60% reported having completed ≥ 3 doses of the hepatitis B vaccination (35). In Africa the coverage was very low the estimated full hepatitis B vaccination coverage was 24.7% (95% CI: 17.3-32.0)(36). In a study on Greek the HBV vaccination coverage of students was high (83%), being higher among medical

students (88.1%, vs. 81.4% among nursing and 80.1% among paramedical students; $p < 0.001$). The vast majority of Greek medical students (95%) have been vaccinated during childhood and 30% of the unvaccinated students declared fear over HBV safety (37). In a study in Georgia the rate of HBV vaccination coverage was 12% and 54% of respondents indicated that they would recommend vaccination to other HCWs (38).

Tetanus, Diphtheria and Pertussis

Tetanus and diphtheria are very serious diseases, luckily were rare in the high-income countries today, but people who do become infected often have severe complications (39). Whooping cough can cause serious illness in babies, children, teens and adults. Symptoms of pertussis usually develop within 5 to 10 days after you are exposed (40). TdPa or TD vaccine (only for booster in adult age) is used to protect adolescents and adults from these diseases.

Benefits and risk in healthcare settings

Recommendations regarding diphtheria vaccine vary across countries for HCWs and the general population (39). In general, there are no specific recommendations for HCWs compared to the general population (see Table 1).

The protection against pertussis (which usually occurs in an oligo-asymptomatic form in adults) is particularly important for the staff of neonatology, paediatrics and obstetrics clinics where contact with infants is frequent and so there is a high risk of transmission of infections (41).

Pertussis outbreaks have been reported from a variety of healthcare settings, including neonatal wards, surgical units and residential homes (42,43). Despite CDC recommended a booster every 10 years transmission has been described from HCWs after vaccination in the previous 3 years, showing a partially effectiveness of vaccination and transmission from HCWs to their patients has been documented (44).

Vaccination coverage

In a recent review the higher initial coverage rate observed was 63.9%, but most studies showed cover-

age rates under 40.0% (8, 45). USA and France are the only two countries with studies evaluating Tdap coverage within HCWs using national data (46–48). In France Pulcini et al. reported a national coverage rate of 63.9% among physicians (49). In a study data from 21 American states using the 2013 Behavioral Risk Factor Surveillance System industry/occupation module were analysed in 2016 with a national coverage of 47.2% (range:38.8– 56.7%) while another study in 2014 showed a coverage of 42.4% (95% CI=38.7%, 46.0%) (50). Paranthaman et al described a higher coverage (90%) and reasons for non-acceptance: included having had pertussis infection or vaccination in childhood, fear of adverse effects, being pregnant or a lack of national policy/colleague recommendation (51). In Italy a multicentre cross sectional study showed a vaccination coverage of 29.5% (16).

Globally the same data described for DT were detected for pertussis with a variable range (40–63.9%) (8,45–52). In a recent survey vaccination data showed a value between 78.6% and 96.5% in healthcare workers in maternity and paediatric care (53). A recent cross-sectional study aimed to assess pertussis seroprevalence among healthy healthcare workers in Tunisia detected a seropositivity rate of 11.4% (95% CI 7.4– 15.5) (54). In USA national coverage varied from 38.7 to % 56.7% while, in Italy, the national coverage was 29.5%, according to a national survey (45–52, 16).

Measles, Mumps, Rubella

Mumps, measles and rubella (MMR) are serious diseases that can lead to potentially fatal illness, disability and death. Due to their transmission way the immunization of healthcare workers could be important to avoid several cases of outbreaks, such as described in literature (55,56).

Benefits and risk in healthcare settings

HCWs are estimated to be at 13- to 19-fold greater risk of acquiring measles compared to the general population (57–59).

Even though a safe and cost-effective vaccine is available, in 2017, there were 110 000 measles deaths globally, mostly among children under the age of five.

In 2017, about 85% of the world's children received one dose of measles vaccine by their first birthday through routine health services (60).

Vaccination coverage

In a retrospective epidemiological study of 1060 HCWs, 90.1% were protected against varicella, 65.6% against mumps, 95.6% against rubella and 92.9% against measles (61). Two studies performed in Turkey found a rate of 94% for measles, 98% for rubella and for mumps of 90–91% (62,63). In a study on 1128 HCWs measles and rubella antibodies were detected in 95.4% and 86.2% of the HCW, with 11.9% of females being unprotected against rubella (64). In a cross-sectional study 71% had ever received an MMR and 42% had received the most recent flu vaccination (65).

Vaccination coverage among HCWs in ten countries of Samu-social international sites was 81.3% (66). In a study of Australian HCWs the vaccination coverage was higher for hepatitis B, tetanus and polio than measles (59.8%), mumps (60.7%), rubella (70.5%), influenza (42.1%) or pertussis (58.2%) (67). Another study in Argentina showed a triple or double viral vaccine coverage of 50.32% with higher levels among those workers with a higher level of education and less seniority (68). In a review by the European Center for Disease Control, coverage rates were 43.6% in France and 62.3% in Denmark (69). In a Japanese seroprevalence survey a total of 1811 HCWs were tested, 91.8% were seropositive to measles, 92.1% to mumps, 89.5% to rubella and 96.3% to varicella (70).

In Italy the coverage reported in several studies was very low, under the target required for herd immunity (16, 71–77).

Chickenpox

Chickenpox is a high contagious disease and so healthcare setting are at particular risk of transmission with possible case of outbreak (defined as the occurrence of five or more cases in a specific setting that are epidemiologically linked). Varicella transmission in healthcare settings from HCWs to susceptible patients has been reported, mostly in tropical countries or in HCWs who received only 1 vaccine dose (78,79).

Varicella vaccine coverage depends on vaccine recommendations for people entering the healthcare workforce.

In Turkey the rate was 98% (63,64) while in Japan the rate coverage was 95% (71). In a study on Saudi Arabia previous history of VZV infection was reported by 1303 HCWs of which 262 (13%) had a history of positive test for varicella antibody, and only 44 (2%) had a history of varicella vaccination (80). In Italy we found a vaccine rate under 20%, in line with other studies (16).

Flu

Influenza is a contagious acute viral infection, with a short incubation period, spreading mainly by droplets, and characterized by respiratory and systemic symptoms. Despite the availability of antiviral drugs vaccines remain the most effective tool for preventing flu. Every year the flu vaccine is offered to HCWs in order to prevent the spread of flu to vulnerable patients and to their colleagues and so to protect themselves, their families and their patients (81).

Vaccination coverage among HCWs is low in Europe (generally less than 30%) despite several recommendations. A significant difference comparing data reported in the USA vs. Europe and other countries exists. According to the CDC data report the 2017- 18 flu vaccination coverage among health care personnel was 78.4%, similar to coverage during the 2016- 17 season (78.6%) (82).

In Europe the rate coverage was also variable: in Spain the 2014 European Health Interview Survey for Spain (N = 22,842) found a value of 18.9% immunized HCWs (83).

In Italy a survey in province of Taranto of the 2015/2016 influenza season detected vaccination coverage among the general practitioners of 76.4% (84). Also, in a multicentre study conducted in ten Italian cities the coverage rate detected was 14% (16).

In a survey of 5141 Belgian HCWs from 13 hospitals and 14 nursing homes, the mean vaccination coverage detected by the authors was 40.4% in the hospitals and 45.3% in the nursing homes (85).

In other countries the vaccination coverage was also variable: for example, 88.3% of the participants of a study in Saudi Arabia declared to get vaccine (80).

Conclusion

These findings underline the low vaccine coverage of HCWs in the World and so the importance of mandatory vaccine (86-89). In some Italian regions and also in some countries mandatory vaccine has been introduced but in literature we found some contrasting opinion about this (90-92). The motivations of vaccine hesitancy are many and maybe other studies would help policymakers and stake-holders to shape programs to improve vaccination coverage and the control of infectious diseases through the correct application of guidelines on prevention (93-98).

Furthermore, the prevention of infectious diseases through vaccinations falls within the competence of the Occupational Physicians, a figure of absolute centrality for its traditional role in the complex system of protection of health and safety in the workplace and also for the role of "health promoter" entrusted by Legislative Decree 81/08. So, it is important in this optic the engagement of OP as well as hygienists to ensure adequate vaccination rates as part of an effective nosocomial infection prevention through vaccinations in an age of antimicrobial resistance (99-110).

Conflict of interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

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