



## Serosusceptibility and hesitancy for booster HBV vaccination among health care workers in Italy: A cross-sectional study



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### ABSTRACT

**Background:** Health care workers (HCWs) are at increased risk of exposure to hepatitis B virus (HBV). The most effective prevention measure is vaccination, with a serum hepatitis B surface antibody (HBsAb) titre > 10 mIU/ml considered protective. To date, the sociodemographic and occupational characteristics related to HBV serosusceptibility and factors associated with booster hesitancy remain unclear. Therefore, this study aimed to identify factors associated with maintaining a protective HBsAb titre in a large sample of HCWs and to evaluate factors potentially associated with hesitancy towards vaccine boosters.

**Methods:** A cross-sectional study was conducted among HCWs who underwent a health surveillance visit between 2017 and 2022. If the serum HBsAb titre was < 10 MIU/ml, a vaccine booster dose was offered. Based on their willingness to be vaccinated, employees were classified into three groups: acceptance, hesitation, and refusal. Uni- and multivariable analyses were performed to assess the association of demographic and occupational characteristics with serosusceptibility and attitudes towards vaccination.

**Results:** A total of 1632 (27%) employees were shown to be nonimmune. A lower median age and being a physician were significantly associated with a protective HBsAb titre. A total of 706 nonimmune employees (43.3%) accepted the vaccination, 865 (53%) hesitated, and 61 (3.7%) refused. The median age of those who refused vaccination was significantly higher than that of those who hesitated and those who were vaccinated. Acceptance of vaccination was significantly higher among nurses, while nurse aides hesitated more; among nonmedical graduate staff both hesitation and refusal were higher than expected. In the multivariable analysis, higher age, female sex, and employment as an allied health care professional were shown to be significantly associated with hesitation/refusal, while being born abroad turned out to be protective. **Conclusions:** Our study showed that approximately a quarter of HCWs were not immune to HBV infection, and of these, more than half were hesitant towards or refused the booster dose. The risk of hesitation/refusal was higher with age in women and among allied health care staff. Based on these findings, further studies are needed to prospectively evaluate HBV seroprevalence, vaccination adherence, factors associated with hesitancy, and the effectiveness of health surveillance strategies in a high-risk population susceptible to infection.

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### Introduction

Hepatitis B is a necroinflammatory hepatopathy of varying severity that is caused by infection with the hepatitis B virus (HBV). Persistent infection is often associated with chronic hepatitis, liver cirrhosis, and hepatocellular carcinoma [1], accounting for

approximately 686,000 deaths recorded annually [2]. Several vaccination strategies have been developed over the years and involve cost-benefit and cost-effective interventions. In 1991, the World Health Organisation (WHO) called on all states to introduce an HBV vaccination programme by 1997 [3]. In Italy, HBV vaccination was introduced in 1983 and was initially offered only to high-risk populations. From 1991 onwards, universal vaccination against HBV became mandatory for all infants and for everyone who had turned 12 years of age (born in 1979), keeping childhood vaccination exclusively from 2003 onwards. This vaccination campaign was highly

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effective, and the overall coverage quickly reached 95% of the population [4].

The Italian HBV vaccine schedule consists of the administration of two doses one month apart that serve as a preliminary dose and a booster dose administered six months after the first [3,5]. Having an antibody titre of 10 mIU/ml or higher measured 1–3 months after the administration of the last dose of the primary vaccination cycle is considered a reliable marker of protection against HBV infection [3]. Individuals with an inadequate antibody response after the primary cycle are defined as "nonresponders". Among them, 40–50% do not reach seroconversion after a second vaccination cycle (up to three additional booster doses) and are called 'true non-responders' [6].

Health care workers (HCWs) are among the highest-risk groups for virus transmission. According to WHO data, there are approximately 2 million HBV infections per year among HCWs [7], mainly due to their frequent exposure to blood and other potentially infectious biological materials [8]. Due to the different maintenance of antibody titres, HCWs need to be tested for their immune status as part of health surveillance. Several studies have shown that those who underwent vaccination in childhood are more often negative for the HBsAb titre at the time of the first visit, but after administration of a booster dose, they show marked positivity [9].

Despite the compulsory nature of HBV vaccination, several factors can influence booster hesitancy [10]. According to the SAGE Working Group on Vaccine Hesitancy, vaccine hesitancy "refers to the delay in accepting or refusing vaccination despite the availability of service" [11]. It is a complex and context-specific phenomenon that varies over time and by place and specific vaccine and is influenced by factors such as confidence, complacency, and convenience [12]. However, factors associated with HBV booster hesitancy among health care workers have not yet been explored.

Our study aimed to assess the HBsAb titres of employees in a large health care company and to investigate the sociodemographic and occupational characteristics associated with HBV serosusceptibility. In addition, the secondary objective of the study was to investigate factors associated with HBV booster hesitancy among health care workers.

## Materials and methods

A cross-sectional study was performed in a large Italian health care company. The study setting involves care at four sites: a general hospital, a trauma-orthopaedic centre, an obstetrics-gynaecology hospital and a children's hospital [13]. As of 2022, the health care company had a total of 10,672 employees, including 1931 physicians, 3295 nurses, 1217 nurse aides, 1577 health technicians, and 992 administrative staff. In this setting, health care workers undergo health surveillance visits with protocols and periodicities that vary according to their tasks and occupational risks. In the case of a haemotransmitted/airborne biohazard, employees are tested for immune defence against various pathogens, including HBV, at the time of recruitment by analysing the HBsAb titre.

Data were collected from employee health surveillance records between 2017 and 2022. Demographic (sex, date of birth, municipality of birth), work-related data (working profiles and areas) and immunological status (HBsAb titre, previous HBV vaccination) were collected for each employee.

According to the Italian vaccination policy—mandatory vaccine since 1991 in infants and 12-year-olds—we stratified employees into three groups according to year of birth (born before 1979, between 1979 and 1990, and after 1990). Employees were also stratified according to place of birth, work profile, and area of employment.

Biochemical data on HBsAb titres were categorised according to the values of HBsAb titres at the time of collection: titres less than 10 mIU/ml were considered nonimmune, while titres greater than 10

mIU/ml defined employees as immune. Based on their HBV immunological status, nonimmune employees were offered a second-generation recombinant vaccine dose with a reevaluation after 1–2 months, as needed by the National Vaccine Prevention Plan for individuals at risk of occupational exposure [14].

Based on their willingness to vaccinate, employees were classified into three groups: acceptance, hesitant, and refusal. The hesitant were those who expressed willingness to vaccinate but did not undergo vaccination.

## Statistical analysis

Descriptive data are shown as absolute (n) and relative (%) frequencies for categorical variables and as the mean and standard deviation (SD) or median and interquartile range (IQR), as appropriate, for continuous variables. Chi-square or Fisher's exact test was used to assess the association between categorical variables (sex, period of HBV vaccination, place of birth, work profile and work area) and employee immune status (immune or nonimmune) or the intention of susceptible HCWs to receive the HBV booster dose (acceptance, hesitant, and refusal); post hoc analysis after chi-square tests with adjustment for multiple comparisons was then performed. T-test and analysis of variance (ANOVA) or nonparametric tests, as appropriate, were used to compare continuous variables (age). Multivariable analyses were then carried out used to assess the independent effect of the demographic and work characteristics of susceptible HCWs on their hesitation or refusal of booster vaccination against HBV. Due to the small number of health care workers who refused vaccination and their comparability with those who hesitated, refusing and hesitating employees were analysed together as one group and compared to those who accepted vaccination. In the final logistic regression model, sex (female vs. male), age, birth abroad vs. in Italy and occupation (after excluding the administrative staff) were considered independent variables, while hesitating or refusing the HBV booster vs. accepting it was the dependent variable.

For all tests, the significance level was set at 0.05.

Analyses were performed with STATA 16® (StataCorp College Station, TX, USA: StataCorp LLC).

## Results

Between 2017 and 2022, 6625 employees of the Health Care Company were tested during health surveillance visits. The majority were females (n = 4538, 68.5%), and the mean age was 31.9 years (SD 11.6, median 27.7, IQR 23.9; 37.2). Overall, 1377 (20.8%) were born before 1979 (no HBV vaccination), 1303 (19.7%) between 1979 and 1990 (mandatory HBV vaccination at 12), and 3939 (59.5%) from 1991 onwards (mandatory HBV vaccination for all newborns). For 6 employees, the date of birth was unknown. Of the 6606 employees with available data, 4584 (69.4%) were born in northern Italy, 223 (3.4%) in central Italy, 1343 (20.3%) in southern Italy and the major islands, and 456 (6.9%) were born abroad. Data on the HBsAb titre were available for 6040 employees: 1632 (27%) had a titre less than 10 mIU/ml, 2070 (34.3%) between 10 and 99 mIU/ml, 1631 (27%) between 100 and 999 mIU/ml, and 707 (11.7%) of 1000 mIU/ml or more. Table 1 shows the demographic and work characteristics of employees stratified by their immune status.

Overall, 1632 (27%) employees were considered nonimmune, and 4408 (73%) immune. Statistically significant associations were observed for the immune status of employees with age, HBV immunisation policy periods, work profile and work area. No significant associations were observed with sex and place of birth.

Following the determination of the HBsAb titres, the booster dose was offered to the 1632 nonimmune employees, who were then stratified into three categories based on their intention to receive the

**Table 1**  
Immune status according to demographic and working characteristics.

HCW characteristics*	Immune (n = 4408)	Nonimmune (n = 1632)	p-value
<b>Female sex</b> n (%)	3008 (68.2)	1108 (67.9)	0.797
<b>Median age</b> , years (IQR)	26.8 (20.9;44)	28 (25.3;35.5)	0.0001
<b>HBV immunisation policy periods</b> n (%)			< 0.001
Born before 1979	770 (17.5)	452 (27.7)	
Born between 1979 and 1990	1045 (23.7)	159 (9.8)	
Born after 1990	2592 (58.8)	1018 (62.5)	
<b>Place of birth</b> n (%)			0.231
Northern Italy	3038 (69)	1134 (69.8)	
Central Italy	150 (3.4)	60 (3.7)	
Southern Italy	894 (20.3)	337 (20.7)	
Abroad	320 (7.3)	94 (5.8)	
<b>Working profile</b> n (%)			< 0.001
Physician/resident	1817 (42)	445 (28.3)	
Nurse/midwife	1259 (29.1)	429 (27.3)	
Nurse aides	469 (10.8)	210 (13.4)	
Nonmedical graduate staff	47 (1.1)	33 (2.1)	
Allied health care professions	675 (15.6)	399 (25.4)	
Administrative staff	62 (1.4)	55 (3.5)	
<b>Work area</b> n (%)			< 0.001
Medicine-pediatrics	1313 (33.7)	354 (25.9)	
Surgery	859 (22.1)	297 (21.7)	
Emergency-critical care area	566 (14.5)	126 (9.2)	
Diagnostic-ambulatory	441 (11.3)	223 (16.3)	
Others	714 (18.3)	369 (27)	

\* Presence of missing data when stratifying for immune status

vaccination: 706 (43.3%) accepted, 865 (53%) hesitated, and 61 (3.7%) refused. Table 2 shows the characteristics of nonimmune employees stratified by their attitude towards HBV vaccination.

The intention of nonimmune employees to receive vaccination was not associated with sex and place of birth. Statistically significant associations were found with age, work profile, and area. Employees who refused vaccination were significantly older than those who accepted it and those who hesitated (both  $p < 0.001$ ).

The attitude towards vaccination was not significantly different than expected for physicians and allied health care professionals. Significant differences emerged for nurses/midwives, nurse aides, graduate nonmedical staff, and administrative staff (Table 3). Statistically significant differences were also observed in the surgical, diagnostic-ambulatory, and 'other' wards (Table 3).

**Table 2**  
Characteristics of nonimmune employees according to their attitude toward vaccination.

	Nonimmune HCWs (n = 1632)			p-value
	Accepted (n = 706)	Hesitated (n = 865)	Refused (n = 61)	
<b>Female sex</b> n (%)	460 (65.1)	605 (69.9)	43 (70.5)	0.118
<b>Median age</b> , years (IQR)	25.1 (20.2;28.6)	28.6 (22.4;48.6)	55.3 (51.5;59.6)	0.0001
<b>Place of birth</b> n (%)				0.203
Northern Italy	484 (68.6)	607 (84.9)	43 (71.7)	
Central Italy	32 (4.5)	28 (3.9)	0 (0)	
Southern Italy	142 (20.1)	35 (4.9)	16 (26.7)	
Abroad	48 (6.8)	45 (6.3)	1 (1.7)	
<b>Working profile</b> n (%)				< 0.001
Physician/resident	194 (27.9)	236 (28.8)	15 (26.8)	
Nurse/midwife	231 (33.2)	183 (22.3)	15 (26.8)	
Nurse aides	70 (10.1)	130 (15.9)	10 (17.9)	
Nonmedical graduate staff	5 (0.7)	25 (3)	3 (5.4)	
Allied health care professions	195 (28)	192 (23.4)	12 (21.4)	
Administrative staff	1 (0.1)	53 (6.5)	1 (1.8)	
<b>Work area</b> n (%)				< 0.001
Medicine-pediatrics	137 (24.8)	196 (26)	21 (34.4)	
Surgery	151 (27.3)	140 (18.5)	6 (9.8)	
Emergency-critical care area	53 (9.6)	69 (9.1)	4 (6.6)	
Diagnostic-ambulatory	103 (18.6)	100 (13.3)	20 (32.8)	
Others	109 (19.7)	250 (33.1)	10 (16.4)	

**Table 3**  
Attitude toward HBV vaccination of nonimmune Healthcare workers (HCWs) by working profile and work area: post-hoc chi-square for pairwise comparisons.

	Nonimmune HCWs (n = 1632)		
	Accepted (43.3%)	Hesitated (53%)	Refused (3.7%)
<b>Working profile</b> , n (row %)			
Physician/resident	194 (43.6)	236 (53.0)	15 (3.4)
Nurse/midwife	231 (53.9) <sup>a</sup>	183 (42.7) <sup>a</sup>	15 (3.5)
Nurse aides	70 (33.3) <sup>b</sup>	130 (61.9) <sup>b</sup>	10 (4.8)
Nonmedical graduate staff	5 (15.2) <sup>c</sup>	25 (75.8) <sup>c</sup>	3 (9.1) <sup>c</sup>
Allied health care professions	195 (48.9)	192 (48.1)	12 (3.0)
Administrative staff	1 (1.8) <sup>d</sup>	53 (96.4) <sup>d</sup>	1 (1.8)
<b>Work area</b> , n (row %)			
Medicine-pediatrics	137 (38.7)	196 (55.4)	21 (5.9)
Surgery	151 (50.8) <sup>e</sup>	140 (47.1) <sup>e</sup>	6 (2.0)
Emergency-critical care area	53 (42.1)	69 (54.8)	4 (3.2)
Diagnostic-ambulatory	103 (46.2)	100 (44.8) <sup>f</sup>	20 (9.0) <sup>f</sup>
Others	109 (29.5) <sup>g</sup>	250 (67.8) <sup>g</sup>	10 (2.7)

<sup>a</sup>  $p < 0.001$

<sup>b</sup>  $p < 0.001$

<sup>c</sup>  $p = 0.001$

<sup>d</sup>  $p < 0.001$

<sup>e</sup>  $p < 0.001$

<sup>f</sup>  $p < 0.001$

<sup>g</sup>  $p < 0.001$

A significantly higher acceptance was observed among nurses (approximately 54%), while it was significantly lower among nurse aides (33.3%) who hesitated more (approximately 62%) than expected. Only 15.2% of the nonmedical graduate staff accepted the HBV booster, while both hesitation (75.8%) and refusal (9.1%) were significantly higher than expected. In surgical wards, acceptance of vaccination was found significantly higher (approximately 51%), while in diagnostic-ambulatory wards refusal was about three times higher than expected (9%).

Because the hesitant and refusing HCWs were significantly different only in median age ( $p < 0.001$ ) and because of the small number of refusing HCWs, the hesitant employees and those who refused the HBV booster dose were considered a single group in the logistic regression analysis and compared with those who accepted the vaccination. The final multivariable model (Table 4) showed a significantly higher risk of hesitation or refusal among older individuals (OR=1.07; 95% CI 1.05, 1.08,  $p < 0.001$ ), females (OR=1.32; 95% CI 1.04, 1.67,  $p = 0.022$ ) and allied health care professionals

**Table 4**  
Odds ratios (OR, CI 95%) of hesitation/refusal of booster vaccination against HBV among nonimmune healthcare workers.

	Hesitant/refusal (n = 926)	
	OR (CI 95%)	p-value
<b>Age</b>	1.07 (1.05; 1.08)	< 0.001
<b>Sex</b> (female vs male)	1.32 (1.04; 1.67)	0.022
<b>Place of birth</b> (abroad vs Italy)	0.61 (0.38; 0.96)	0.035
<b>Working profile</b>		
Physician/resident	Ref	-
Nurse/midwife	0.91 (0.67; 1.22)	0.511
Nurse aides	0.69 (0.46; 1.03)	0.067
Nonmedical graduate staff	1.66 (0.60; 4.55)	0.325
Allied health care professions	1.43 (1.05; 1.93)	0.021

compared to physicians (OR=1.43; 95% CI 1.05, 1.93,  $p = 0.021$ ), while foreign-born employees showed a significantly lower risk compared with Italian-born employees (OR=0.61; 95% CI 0.38, 0.96,  $p = 0.035$ ). Finally, being a nurse/midwife, a nurse aide or a nonmedical health worker did not show a significantly different risk of hesitation/refusal than physicians.

## Discussion

This study aimed to assess HBsAb titres in a large health care company whose employees underwent health surveillance visits between 2017 and 2022 and to investigate the sociodemographic characteristics involved in their different immunological responses. In addition, our aim was to evaluate factors associated with hesitation towards the HBV vaccine in HCWs.

In our sample, the overall prevalence of individuals without circulating HBsAb was 27%. This finding is consistent with a recent systematic review and meta-analysis by Bianchi et al. [15], who analysed the rate of hepatitis B serosusceptibility among HCWs in nearly 25,000 Italian HCWs and reported an overall prevalence of hepatitis B serosusceptibility of 27%. In addition, our results showed statistically significant associations between immune status, age, and HBV immunisation policy period. In our sample, approximately 28% of those who had received mandatory vaccination under the national vaccination plan since 1991 were observed to be non-immune, compared with 13% of those born between 1979 and 1990 who were likely to have been vaccinated at age 12. In this regard, it should be considered that most of our immunological data came from preemployment visits of workers born since 1991 (60% of our sample) and who most likely had not received any booster dose since childhood. Our results are in agreement with other studies that have reported a higher prevalence of circulating antibodies in individuals vaccinated during adolescence and adulthood than in those vaccinated in childhood [16,17]. This finding could be explained by a lower immunogenicity of the HBV vaccine administered to infants than to adolescents or adults due to the different maturity of the immune system of these groups [9,15,18]. In contrast, our results did not find an association between sex and the immunological status of employees. In this regard, there is conflicting evidence in the scientific literature: several studies report no statistically significant differences between men and women [19,20], while others have shown greater serosusceptibility among males [18,21].

Lower antibody titres can be observed according to work areas or work profiles. In particular, workers not engaged in hands-on activities or employed in work areas at low risk of exposure have higher serosusceptibility. Accordingly, a study by Garzillo et al. [7] showed that nurses and health care workers at higher risk of exposure had higher HBsAb titres than other health care professionals. These authors hypothesised that this might be due to more direct and frequent contact with contagious patients and their body fluids

compared to other HCWs. After titre assessment, more than half of the staff hesitated to receive the booster dose even though they were not immune. Factors associated with vaccine hesitancy were age, sex, work profile, and place of birth. Factors associated with HBV booster hesitancy have not been thoroughly explored in the current scientific literature. In fact, this topic has gained increasing relevance during the COVID-19 vaccination campaign. In this regard, the attitudes of HBV and COVID-19 towards booster doses seem to be different. Our findings showed that a higher median age and female sex were associated with a higher risk of hesitancy. In contrast, other studies [22,23] have recently shown that willingness to undergo a booster dose of COVID-19 was lower for men and younger people.

Regarding occupational profiles, allied health care professionals showed a higher rate of hesitation after controlling for confounding factors. The perception of being less exposed to infectious agents and occupational risks, such as needlestick and sharp injuries, may have influenced their response to the proposed booster. Employees working in high-risk settings usually show a greater propensity to accept vaccinations [24]. Regarding place of birth, foreign-born employees showed greater willingness to receive the booster dose. This difference could be attributed to the "3Cs model" by the "SAGE Working Group on Vaccine Hesitancy". Namely, attitudes towards vaccination may be influenced by factors such as cultural background, the possibility of being vaccinated, and the quality of vaccination service. As a result, foreign-born HCWs may be more sensitive to vaccination campaigns proposed by the Occupational Service.

The results of our study may have several implications for improving the health and safety of health care workers. Awareness of significant differences in antibody titres and vaccine adherence could allow the creation of individualised interventions. Specifically, it is of utmost importance to create multicomponent interventions to increase HBV vaccination adherence. In fact, the literature shows that successful interventions should include as many components as possible [25,26]. According to our results, one of the components should be aimed at improving knowledge of the long-term health effects of HBV infection, especially to HCWs with a lower level of health literacy. In this context, the role of occupational physicians and nurses is to exploit mandatory health surveillance visits to tailor health promotion activities. In addition, groups with a higher willingness to undergo HBV vaccination could be identified for the selection of peer health educators. It has been suggested that the role of peer health educators is an important component of multilevel workplace interventions to promote healthy behaviours and to encourage behavioural changes. Due to the magnitude of the problem and its health implications, these efforts should be largely encouraged by policymakers and health authorities.

The main strength of this study is that it addresses factors influencing willingness to receive booster vaccination for HBV in a high-risk population susceptible to infection. Moreover, it analysed data collected from a large sample of HCWs over a 5-year period. However, our study also has some limitations. The main limitation is the cross-sectional nature of the study design, which does not allow us to draw conclusions about causality; in addition, analyses on health surveillance data allowed us to investigate only some sociodemographic and occupational aspects that might be associated with attitudes towards vaccination. Another limitation is the unknown adherence of employees to previous vaccination schedules; however, considering that HBV vaccination became mandatory in Italy in 1991, we can assume that most of our sample completed the vaccination cycle. Future research should evaluate all factors included in the "3Cs" model by the "SAGE Working Group on Vaccine Hesitancy". In addition, future studies should focus on the determinants of true non-responders to target interventions and implement effective health surveillance strategies.



## Conclusions

Our study showed that approximately a quarter of the health care workers were nonimmune to HBV infection. In addition, workers not engaged in hands-on activities or employed in work areas at lower risk of exposure showed higher serosusceptibility. Among non-immune HCWs, more than half hesitated or refused the booster dose. This study identified factors associated with HBV booster hesitation in HCWs: increasing age, female sex, and employment as allied health care professional were shown to be significantly associated with hesitancy; in contrast, being born abroad was protective.

Due to the high prevalence of HBV infection and nonimmune HCWs, these findings are of utmost importance to target future interventions to reduce vaccine booster hesitancy and to implement specific health surveillance strategies for true nonrespondents. To address these issues, future studies should prospectively assess HBV seroprevalence, vaccination adherence, and the effectiveness of implemented interventional strategies.

## Declaration of Competing Interest

We have no conflict of interest to declare.

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