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Web-based analysis of adherence to influenza vaccination among French healthcare workers.

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Background.

Influenza is an annual public health concern that is responsible for two to five million severe infections and between 290,000 to 650,000 deaths worldwide. There is high influenza morbidity and mortality especially in at-risk patients (aged over 65 years and/or patients with chronic diseases). Recently, in France, influenza had a very high impact in ~~on~~ the elderly (11,400 and 14,300 estimated deaths related to influenza infection during 2014-2015 and 2016-2017, respectively), especially due to outbreaks seen in nursing homes [1,2]. To reduce this impact and burden, French national authorities took action to promote influenza vaccination programs [3]. Every year from October to January, a vaccination campaign is organized and a vaccine voucher is sent by the French National Health System (CNAMTS) to nearly ten million at-risk or frail patients [4].

In addition, all those in contact with these at-risk individuals,—such as healthcare workers (HCWs), are also urged to receive the vaccine. HCW vaccination can improve indirect protection through herd immunity and has an educational role on collective vaccination benefits. However, despite the frequent description of nosocomial outbreaks due to HCW-to-patient transmission in nursing homes or hospitals, numerous studies have reported low vaccine uptake within the HCW population [5]. Influenza infection in HCWs is also a major reason for absenteeism in the hospital during winter, increasing the influenza burden.

As a result, the World Health Organization (WHO), the Centers for Disease Control and Prevention (CDC and ECDC) and the Public Health Institutes recommend that -all HCWs receive annual influenza vaccination [6]. However, despite this recommendation, influenza vaccine uptake among HCWs remains low in European countries. In 2014, for the 10 EU countries that

could provide data on HCW vaccination rates, the vaccine uptake reported was less than 35%, similar to in France[7–10].

According to previous studies, vaccine hesitancy from French HCWs is fuelled by adverse messages that described both negligible vaccine effectiveness and high risk for severe side effects [11]. As a result, the implementation of mandatory HCW vaccination has been suggested by policy makers as an effort to increase influenza vaccine uptake [12].

Objectives.

This study aimed to test a web-based tool that provided a very rapid national picture about ~~on the~~ influenza vaccine uptake among active or retired HCWs in France. In addition to the analysis of the demographic and professional factors associated with vaccine uptake, we also tested the potential adherence to a mandatory influenza vaccination programme for HCWs.

Study design.

A standardized e-survey (14 closed-ended questions) was prepared. Nationwide mailing lists of HCWs were provided by professional physician, pharmacist, nurse and physical therapist councils. The French vaccination campaign ended on January 31 and the e-survey was e-mailed to all HCWs (without exclusion) on February 1, 2017 with a reminder e-mail on February 15, 2017, using a secured electronic platform developed for this purpose. HCWs were invited to answer the questions anonymously. To optimize coverage of the targeted population, the survey was also sent to the regional organization of care/nursing homes (“Federation des Maisons et des Pôles de Santé”). (Suppl. Figure 1).

Statistical analysis

Answers were considered after 3,000 complete replies were recorded (the sample size was determined from an unpublished study to obtain at least a power of 0.99 for testing vaccination status). Statistical analyses and representations were performed using Epi Info™ 7 (Epi Info Software, CDC, Atlanta, GA, USA) and/or GraphPad Prism software (V7.0) (GraphPad Software Inc, La Jolla, CA, USA). The Mann-Whitney or Kruskal-Wallis statistical tests were used for quantitative variables (adherence to mandatory vaccination), while the Fisher Exact test was used for qualitative variables (all variables but adherence). Results were significant when the p-value (p) was < 0.05.

Ethical consideration

All responders were de-identified prior to statistical analysis and no metadata subset was collected during the study. Because of this design, the study did not need approval by an ethics board and all participants were informed about the objectives and the study method. Submitting the questionnaire was considered as agreeing consensual to the terms of the study.

Results.

Thousands of emails were sent during the two rounds of emails on February 1 and 15. On February 16, 6,250 HCWs had connected to the e-survey and 3,000 complete answers were collected, corresponding to a 48% conversion rate. The subsequent analysis was carried out from those 3,000 answers. All the characteristics used for the following analysis were included in

Figure 1.

Cohort characteristics

The global sex ratio (F/M) was 2.77. Amongst the 3,000 answers, 1,944 were collected from nurses (64.8%); 436 from physicians (14.5%); 305 from pharmacists (10.2%) and 220 from physical therapists (7.3%). The proportion of each professional category that answered the questionnaire was not statistically different compared to the global representation of HCWs in France ($p>0.05$) (**Table 1**). Only 95 answers came from administration or an unspecified work category (95/3,000; 3.1 %). These were excluded from the analysis to focus on HCWs.

HCWs who responded were mostly active ($n=2,782/2,905$; 95.8%). Among these HCWs, 2,750 answered the question on the type of practice (community-based or hospital-based or mixed practice): 62.9% had a community-based practice (1,729/2,750) *versus* 28.3% with a hospital-based practice (779/2,750) and 8.8% with a mixed practice (242/2,750) ($p<0.01$). Overall, 92.1% of all active HCWs declared taking care of at-risk patients ($n=2,563/2,782$), including elderly patients (88.5%; $n=2,268/2,563$), patients with chronic diseases, *i.e.* needing regular medical consultation (70.0%; $n=1,793/2,563$), immunocompromised patients, *i.e.* with immune disorders or immunosuppressive therapies, (51.3%; $n=1,316/2,563$), and or others [children ($n=810/2,563$; 31.6%), pregnant women ($n=19/2,563$; <1%); ICU cases ($n=11/2,563$, <1%) and disabled patients ($n=18/2,563$; <1%)]. Respective proportions of patients' risk groups per HCW professional category are presented in **Figure 2**, and respective age distribution in **Suppl. Figure 2**.

Most were in urban areas ($n=2,155/2,905$; 74.2%; $p<0.01$), including 37.7% in small-sized cities of less than 50,000 inhabitants ($n=811/2,155$).

Vaccine uptake during the current season

Overall, 45.7% (1,327/2,905) of HCWs declared being vaccinated against influenza for the 2016-17 season. Vaccine uptake was statistically correlated to professional status ($p<0.01$), age ($p<0.01$), and practice ($p<0.01$), as reported in **Figures 3** and **4**. Briefly influenza vaccination coverage ranged from 23.2% for the physical therapists (51/220) to 75.2% for the physicians (328/436) ($p<0.01$); the vaccine uptake for the pharmacists and nurses was 59.3% (181/305) and 39.5% (767/1,944) respectively. Regardless of professional status, vaccine uptake increased with age from 22.3% (105/470) for the 20- to 30-year-old age group to 69.9% (200/286) for the 61+-year-olds ($p<0.01$) (Supplementary figure 4). Higher vaccine uptake was reported by HCWs with in community-based practices (47.2% *versus* 40.2%; $p<0.01$); HCWs in both practice types, community and hospital, reported an intermediate vaccination rate (43.9%).

As expected, vaccination during the current year (2016-2017) was significantly associated with previous influenza vaccination (96.0% *versus* 32.2%; $p<0.01$) or willing to be vaccinated during the next season (98.5% *versus* 13.8%; $p<0.01$).

Insight into mandatory vaccination

Responders were asked if they agreed with implementing mandatory influenza vaccination for HCWs. Responses ranged from 1 (“not at all”) to 10 (“absolutely yes”). Overall, 2,905 answers were taken into account. Among all, the median response value was 5 (interquartile range IQR=8) with a bimodal distribution toward the extreme scores. Regardless of the professional status, accepting mandatory influenza vaccination increased with age, with the median score progressing gradually from 2 (IQR=7; 20-30 years age group) to 9 (IQR=6.25; 61+ age group) ($p<0.01$). In addition, significant differences were also observed between the 4 professional statuses. Physical therapists were less likely to accept mandatory vaccination (median 1; IQR=4)

than physicians or pharmacists (median 8; IQR=5 and median 9; IQR=4, respectively; $p<0.01$).

Nurses had an intermediate median score (median 4; IQR=7). These results are summarized in

Figure 3 (and Suppl. Figure 3).

Neither handling at-risk patients (median 5; IQR=8 versus median 4; IQR=8 for HCWs without contact with at-risk patients) nor community-based practice (median 5; IQR=8 *versus* median 4; IQR=7 in hospital-based practice) had any impact on the score. Finally, being vaccinated during the 2016-2017 epidemic season was significantly associated with a higher score for accepting mandatory vaccination (median 9; IQR=3 versus median 1; IQR=3; $p<0.01$).

Among the HCW who were vaccinated during the 2016-2017 epidemic season and regardless of professional status, accepting mandatory influenza vaccination increased with age, with a median score progressing from 8 (IQR=5; 20-30 years age group) to 10 (IQR=2; 61+ age group) ($p<0.01$). This progression was not observed among the HCW who were not vaccinated during the 2016-2017 epidemic season with a median score of 1 for all age categories. In addition, significant differences were observed between the professional groups. Among HCWs vaccinated during the 2016-2017 epidemic season, physical therapists and nurses were less likely to accept mandatory vaccination (median 8; IQR=5 and median 9; IQR=4, respectively) than physicians and pharmacists (median 10; IQR=2 for both category). Among the HCWs who were not vaccinated during the 2016-2017 epidemic season, accepting mandatory influenza vaccination was not different between physicians (median 1; IQR=4), nurses (median 1; IQR=2) and physical therapists (median 1; IQR=2). However, surprisingly, pharmacists who were not vaccinated during the 2016-2017 epidemic season were mainly in favor of accepting mandatory influenza vaccination (median 7; IQR=8) (**Suppl. Figure 4**).

Discussion.

To our knowledge, this web-based study built for rapid estimation of influenza vaccine uptake coupled with feedback on the potential implementation of mandatory influenza vaccination among HCWs at national level is the first of its kind. This survey provided data from a large cohort of HCWs, (number of responses: n=3,000), with a high (48%) and rapid (15 days) conversion rate. Even though our cohort represented only 0.3% of all HCWs registered in France, its size compares very favorably with similar published studies [13,14].

In France, as in other countries, influenza vaccine coverage in HCWs is reported to be low, around 20%. However, the different studies reporting on vaccine uptake showed important disparities (from 0% to 69%) [15]. Our survey reported 45.7% of HCWs being vaccinated (1,327/2,905) for the 2016-17 season, much higher than expected. Disparities and differences between all the studies may be explained by the design of each study. Our study was web-based and answers were only collected over a 15 day period from willing HCWs. Therefore, the results may only reflect the response from the more concerned and connected HCWs. However, as vaccine uptake has an impact in terms of protection as well as vaccine advocacy for the frail patients, minimizing the delay to provide key nationwide data about HCW vaccination rate was considered decisive.

Some of the results were concordant with those already published such as higher vaccine uptake in previously vaccinated HCWs and in community-based practice *versus* hospital-based HCWs [16]. Other studies reported discrepant results compared with ours, such as the lack of gender or age-related differences in influenza vaccine uptake [17–20].

Nevertheless, our study had some limitations. The self-report method could induce a possible recall bias which could impact on the results, especially regarding previous vaccination and date of vaccination as well as the vaccination status and care for at-risk patients. The latter was reported at a very high level (92.1%), precluding any analysis to determine the impact of having this type of patient as a vaccination incentive. In addition, the vaccination status and care for at-risk patients are two parameters highly influenced by a social desirability bias, which was not evaluated in this study either. Moreover, no independent verification could be set up, as responses were anonymously obtained to protect the HCW identity [19]. In our study, it was not tested whether, as reported by Khan *et al.*, there was a difference about the perception of influenza burden and on influenza vaccination in relation to their professional experience or recent training [18]. This specific question could be included in the next survey to see if such training could influence vaccine uptake.

Regardless of profession, omission and opposition were the two main reasons for non-vaccination in HCWs. Omission could be easily overcome by simplifying the access to vaccination through (i) de-centralizing vaccination centers, (ii) information on influenza and on vaccine availability and (iii) free access to the vaccine and incentives for HCWs [20–23]. Vaccine opposition is more difficult to overcome, especially since HCWs should be more informed/educated on this subject than the general population. The emergence of “alternative medicine” has fuelled the negative messages against vaccines blamed for supposed adverse events. Reports showed that this kind of misinformation might be conveyed by HCWs with outdated information and training [24].

As a result, policy makers may be willing to implement mandatory influenza vaccination. This is supported by the very high vaccine uptake observed in HCWs from structures that implemented this mandatory vaccination policy [6,25]. High HCW influenza vaccination uptake is supposed to

provide a protective herd immunity effect for frail patients. However, it has not been demonstrated that it required 100% of vaccination; 80% or 60% has been hypothesized to be enough [26]. On one hand, convincing HCWs by defining realistic objectives (*i.e.* at least 60% or 80% vaccination coverage) instead of imposing vaccination could promote an educational approach, which could be useful for all vaccination programmes. On the other hand, setting a new normative standard that included mandatory influenza vaccination could also change the perception about both the influenza burden and the need for optimal prevention. Therefore, both attitudes could be beneficial and would require implementation of a comprehensive annual campaign organized by the public health authorities to convince HCWs about the relevance of being vaccinated against influenza, with clear objectives and expected outcomes [5]. In addition, our study revealed that HCWs already vaccinated against influenza were more in favor of mandatory vaccination. Therefore, we should remember that convincing ~~the~~ HCWs will also reduce vaccine hesitancy in the general population.

Surveys on the perception and usage of influenza vaccines ~~and~~ are important when considering influenza vaccination in HCWs. The surveys were easy to perform and should be carried out more frequently. Over a 3 weeks period, our web-based study identified specific HCW groups that were less likely to be vaccinated. Repeat surveys would help to evaluate the impact of educational health messages and identify those adapted for each professional category. This way, disease burden could be reduced by increasing vaccine uptake in HCWs and subsequently in the general population through better knowledge and awareness about influenza and its prevention.

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Conflict of interest statement:

M.P. received a grant from Theradiag and Hologic to attend clinical microbiology conferences (RICAI, ESCV conference meetings).

A.G. received a travel grant from Cobas to attend the RICA 2017 Conference.

M.V. received a grant from Theradiag to attend the ESCV 2017 Conference.

B.L. received travel grants to attend meetings from GSK and Sanofi Pasteur. B.L is the Chair of the scientific committees of Immuniser Lyon, the GIRI and GHISN. All personal remuneration stopped in September 2010.

F.S., C.B. and H.Z. collaborated with the pharmaceutical and vaccine industry (consultant specialized in healthcare).

None of these potential conflicts of interest were implicated in the design of this study, or the analyses of the results, nor the decision to publish.

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Author contribution:

M.P. and A.G analyzed and interpreted the data as well as drafted and reviewed the article; C.B and H.Z enabled the acquisition of data; M.V. critically revised the article for important

intellectual content; F.S. and B.L conceived, and designed the study in addition to critically
revising the article for important intellectual content.

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Figure and table

Figure 1. Flow chart of responders included in this study.

Figure 2. Distribution of HCW taking care of at-risk patients through at-risk patients categorization. Each of the four main at risk patient categories is represented on the abscissa axis. The respective percentage of each HCW taking care of at-risk patients is expressed on the ordinate axis. The “other” category groups together with children (before 16 years old), pregnant women, patients hospitalized in intensive care unit or severely disabled individuals.

Figure 3. Perception of mandatory influenza vaccination per HCWs professional category.

The HCW agreement to the mandatory influenza vaccination was graduated using a scale from 1 (“not at all”) to 10 (“absolutely yes”). Proportions of active HCW categories with a grade corresponded to the X-axis. Physical therapists and nurses were significantly less supportive than physicians and pharmacists ($p < 0.001$), with an important proportion of the active responders (40% and 50% of nurses and physical therapists respectively) giving a “not at all” agreement to mandatory vaccination.

Table 1. Respective proportion of HCW categories, in France and in the responders’ cohort.

Supplementary figures

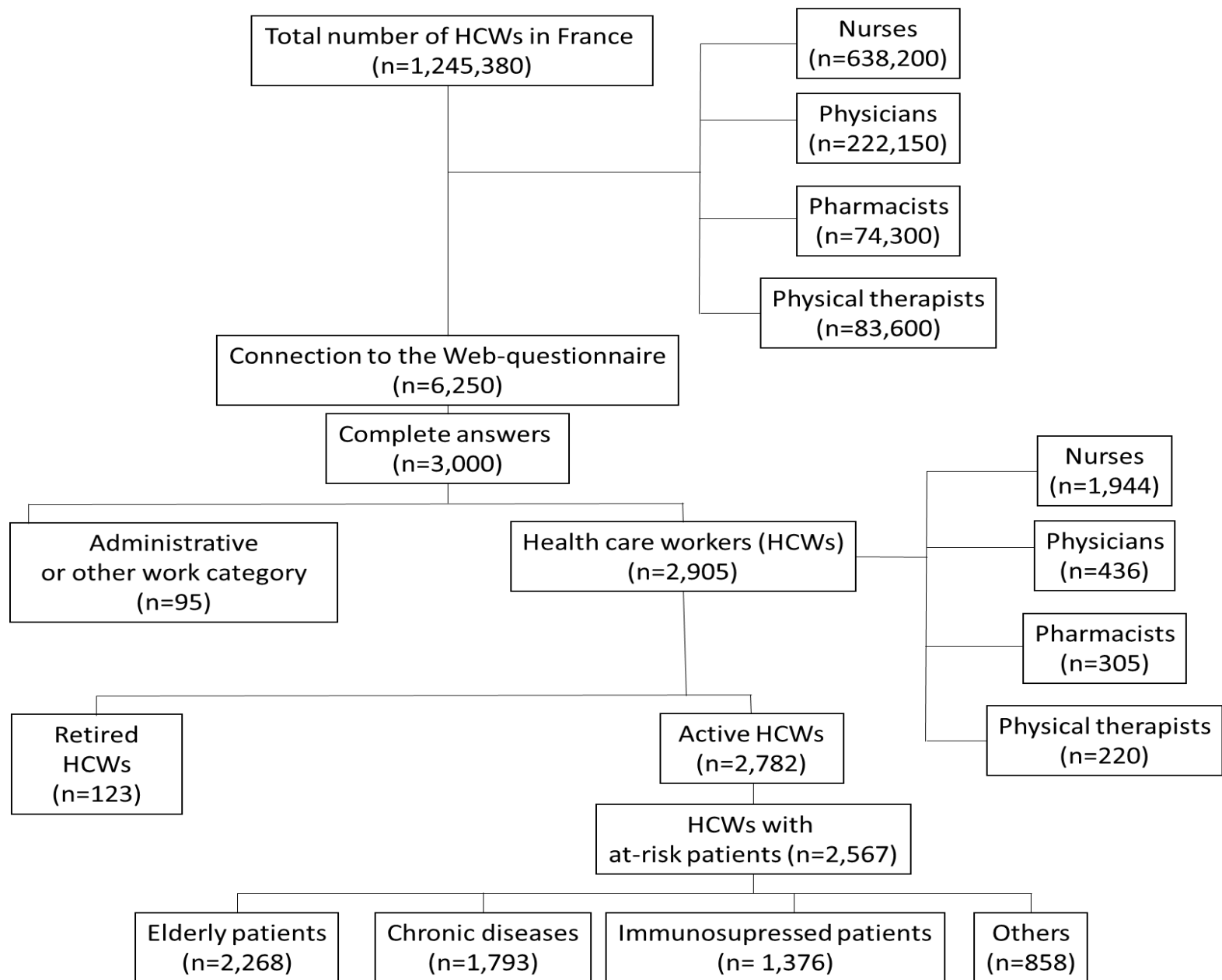
Supplementary figure 1. Electronic questionnaire submitted to the responders. Each of the 14 questions was translated thereafter. 1- Indicate your profession; 2- Are you retired?; 3- What type of patients do you take care of?; 4- Do you work at hospital? ; 5- How do you work (alone or with other HCWs)?; 6-Where do you work?; 7- Are you a man or a woman?; 8-How old are you?; 9- Have you been vaccinated against influenza (epidemiological season 2016-2017)?; 10- When were you vaccinated during this epidemiological season?; 11- Have you already been vaccinated against influenza before?; 12- Will you be vaccinated next year (epidemiological season 2017-2018)?; 13- What do you think of the mandatory vaccination against influenza for HCWs?; 14- Do you think that mandatory vaccination has to be applied solely to HCWs taking care of at-risks patients?

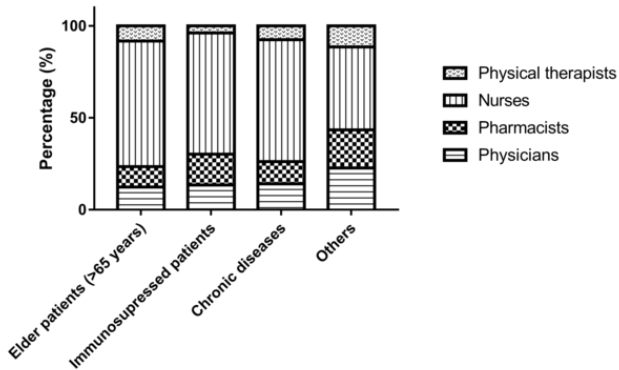
Supplementary figure 2. Age distribution of the responders per HCW category

Supplementary figure 3. Adherence to mandatory vaccination against influenza stratified by HCWs category and age.

Supplementary figure 4. Adherence to mandatory vaccination against influenza stratified by age (A) or HCW category (B). Results obtained among HCW who were vaccinated during the 2016-2017 epidemic are represented in grey and results obtained among HCW who were not vaccinated during the 2016-2017 epidemic are represented in black. Results are represented by a box plot with min and max.

Supplementary Table 1. Vaccine coverage in 2016 - 2017 according to the care of at-risk patients per HCW category.





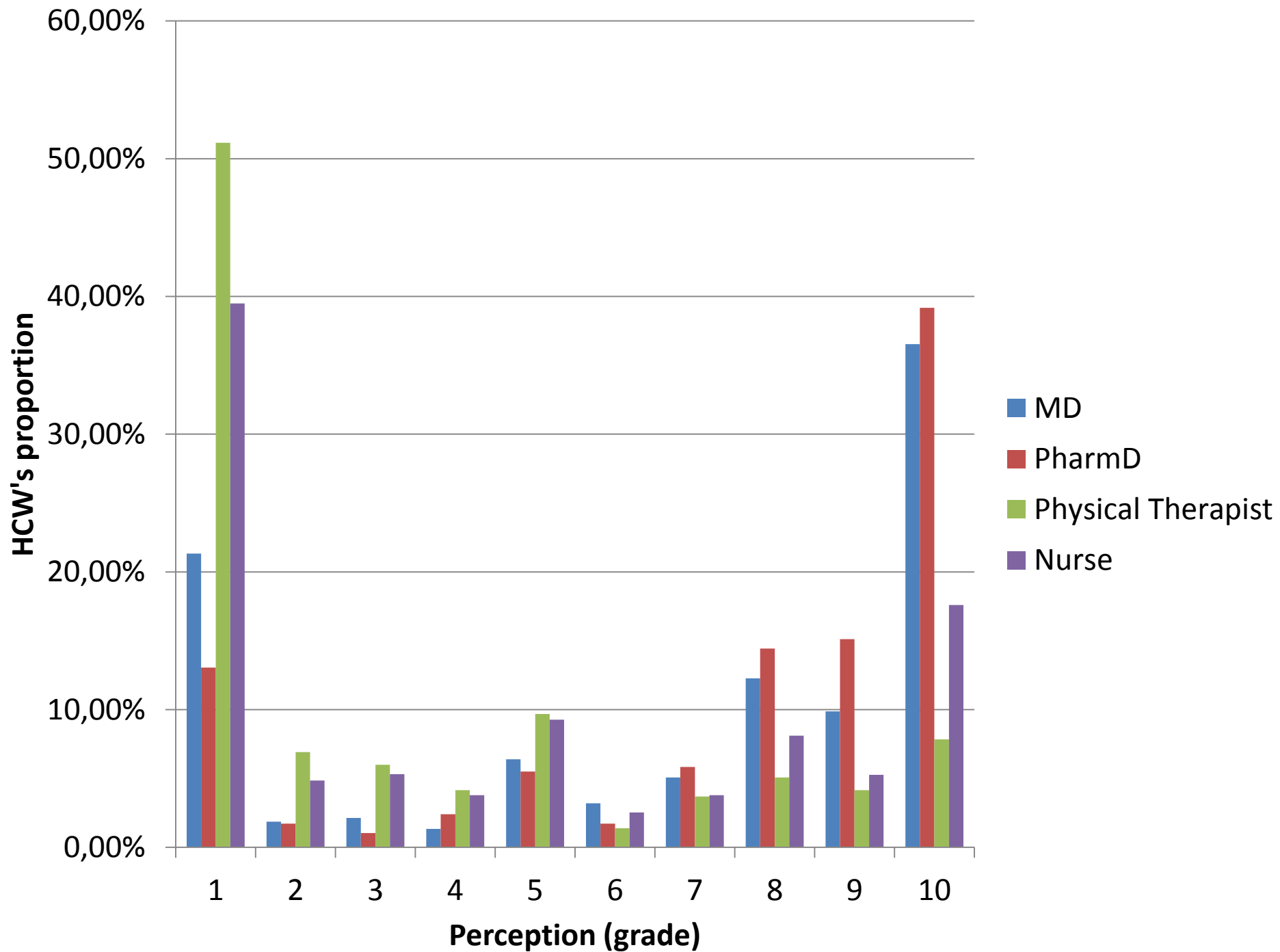


Table 1. Respective proportion of HCW categories, in France and in the responders' cohort.

HCWs Categories	Respective number of HCWs	% of each HCWs (in France)*	% of each HCWs (in responders' cohort)
Nurses	638,200	51.2	64.8
MD	222,150	17.8	14.5
Physical therapists	83,600	6.7	7.3
PharmD	74.,300	6.0	10.2
Total	1,245,380	100	100

* adapted from [27]