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

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1 **Background.**

2 Influenza is an annual public health concern that is responsible for two to five million severe
3 infections and between 290,000 to 650,000 deaths worldwide. There is high influenza morbidity
4 and mortality especially in at-risk patients (aged over 65 years and/or patients with chronic
5 diseases). Recently, in France, influenza had a very high impact in ~~on~~ the elderly (11,400 and
6 14,300 estimated deaths related to influenza infection during 2014-2015 and 2016-2017,
7 respectively), especially due to outbreaks seen in nursing homes [1,2]. To reduce this impact and
8 burden, French national authorities took action to promote influenza vaccination programs [3].
9 Every year from October to January, a vaccination campaign is organized and a vaccine voucher
10 is sent by the French National Health System (CNAMTS) to nearly ten million at-risk or frail
11 patients [4].

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

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

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

25 According to previous studies, vaccine hesitancy from French HCWs is fuelled by adverse
26 messages that described both negligible vaccine effectiveness and high risk for severe side effects
27 [11]. As a result, the implementation of mandatory HCW vaccination has been suggested by
28 policy makers as an effort to increase influenza vaccine uptake [12].

29 **Objectives.**

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

34 **Study design.**

35 A standardized e-survey (14 closed-ended questions) was prepared. Nationwide mailing lists of
36 HCWs were provided by professional physician, pharmacist, nurse and physical therapist
37 councils. The French vaccination campaign ended on January 31 and the e-survey was e-mailed
38 to all HCWs (without exclusion) on February 1, 2017 with a reminder e-mail on February 15,
39 2017, using a secured electronic platform developed for this purpose. HCWs were invited to
40 answer the questions anonymously. To optimize coverage of the targeted population, the survey
41 was also sent to the regional organization of care/nursing homes (“Federation des Maisons et des
42 Pôles de Santé”). (**Suppl. Figure 1**).

43 *Statistical analysis*

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

52 *Ethical consideration*

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

57 **Results.**

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

62 **Figure 1.**

63 *Cohort characteristics*

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

70 HCWs who responded were mostly active ($n = 2,782/2,905$; 95.8%). Among these HCWs, 2,750
71 answered the question on the type of practice (community-based or hospital-based or mixed
72 practice): 62.9% had a community-based practice (1,729/2,750) *versus* 28.3% with a hospital-
73 based practice (779/2,750) and 8.8% with a mixed practice (242/2,750) ($p < 0.01$). Overall, 92.1%
74 of all active HCWs declared taking care of at-risk patients ($n = 2,563/2,782$), including elderly
75 patients (88.5%; $n = 2,268/2,563$), patients with chronic diseases, *i.e.* needing regular medical
76 consultation (70.0%; $n = 1,793/2,563$), immunocompromised patients, *i.e.* with immune disorders
77 or immunosuppressive therapies, (51.3%; $n = 1,316/2,563$), and or others [children ($n = 810/2,563$;
78 31.6%), pregnant women ($n = 19/2,563$; <1%); ICU cases ($n = 11/2,563$, <1%) and disabled
79 patients ($n = 18/2,563$; <1%)]. Respective proportions of patients' risk groups per HCW
80 professional category are presented in **Figure 2**, and respective age distribution in **Suppl. Figure**
81 **2**.

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

84 *Vaccine uptake during the current season*

85 Overall, 45.7% (1,327/2,905) of HCWs declared being vaccinated against influenza for the 2016-
86 17 season. Vaccine uptake was statistically correlated to professional status ($p<0.01$), age
87 ($p<0.01$), and practice ($p<0.01$), as reported in **Figures 3** and **4**. Briefly influenza vaccination
88 coverage ranged from 23.2% for the physical therapists (51/220) to 75.2% for the physicians
89 (328/436) ($p<0.01$); the vaccine uptake for the pharmacists and nurses was 59.3% (181/305) and
90 39.5% (767/1,944) respectively. Regardless of professional status, vaccine uptake increased with
91 age from 22.3% (105/470) for the 20- to 30-year-old age group to 69.9% (200/286) for the 61+-
92 year-olds ($p<0.01$) (Supplementary figure 4). Higher vaccine uptake was reported by HCWs with
93 in community-based practices (47.2% versus 40.2%; $p<0.01$); HCWs in both practice types,
94 community and hospital, reported an intermediate vaccination rate (43.9%).

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

98 *Insight into mandatory vaccination*

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

107 than physicians or pharmacists (median 8; IQR=5 and median 9; IQR=4, respectively; $p<0.01$).
108 Nurses had an intermediate median score (median 4; IQR=7). These results are summarized in
109 **Figure 3 (and Suppl. Figure 3)**.

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

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

129 **Discussion.**

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

136 In France, as in other countries, influenza vaccine coverage in HCWs is reported to be low,
137 around 20%. However, the different studies reporting on vaccine uptake showed important
138 disparities (from 0% to 69%) [15]. Our survey reported 45.7% of HCWs being vaccinated
139 (1,327/2,905) for the 2016-17 season, much higher than expected. Disparities and differences
140 between all the studies may be explained by the design of each study. Our study was web-based
141 and answers were only collected over a 15 day period from willing HCWs. Therefore, the results
142 may only reflect the response from the more concerned and connected HCWs. However, as
143 vaccine uptake has an impact in terms of protection as well as vaccine advocacy for the frail
144 patients, minimizing the delay to provide key nationwide data about HCW vaccination rate was
145 considered decisive.

146 Some of the results were concordant with those already published such as higher vaccine uptake
147 in previously vaccinated HCWs and in community-based practice *versus* hospital-based HCWs
148 [16]. Other studies reported discrepant results compared with ours, such as the lack of gender or
149 age-related differences in influenza vaccine uptake [17–20].

150 Nevertheless, our study had some limitations. The self-report method could induce a possible
151 recall bias which could impact on the results, especially regarding previous vaccination and date
152 of vaccination as well as the vaccination status and care for at-risk patients. The latter was
153 reported at a very high level (92.1%), precluding any analysis to determine the impact of having
154 this type of patient as a vaccination incentive. In addition, the vaccination status and care for at-
155 risk patients are two parameters highly influenced by a social desirability bias, which was not
156 evaluated in this study either. Moreover, no independent verification could be set up, as responses
157 were anonymously obtained to protect the HCW identity [19]. In our study, it was not tested
158 whether, as reported by Khan *et al.*, there was a difference about the perception of influenza
159 burden and on influenza vaccination in relation to their professional experience or recent training
160 [18]. This specific question could be included in the next survey to see if such training could
161 influence vaccine uptake.

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

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

173 provide a protective herd immunity effect for frail patients. However, it has not been
174 demonstrated that it required 100% of vaccination; 80% or 60% has been hypothesized to be
175 enough [26]. On one hand, convincing HCWs by defining realistic objectives (*i.e.* at least 60% or
176 80% vaccination coverage) instead of imposing vaccination could promote an educational
177 approach, which could be useful for all vaccination programmes. On the other hand, setting a
178 new normative standard that included mandatory influenza vaccination could also change the
179 perception about both the influenza burden and the need for optimal prevention. Therefore, both
180 attitudes could be beneficial and would require implementation of a comprehensive annual
181 campaign organized by the public health authorities to convince HCWs about the relevance of
182 being vaccinated against influenza, with clear objectives and expected outcomes [5]. In addition,
183 our study revealed that HCWs already vaccinated against influenza were more in favor of
184 mandatory vaccination. Therefore, we should remember that convincing ~~the~~ HCWs will also
185 reduce vaccine hesitancy in the general population.

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

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204 F.S., C.B. and H.Z. collaborated with the pharmaceutical and vaccine industry (consultant
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212 **Author contribution:**

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

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

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304 **Figure and table**

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

306 **Figure 2. Distribution of HCW taking care of at-risk patients through at-risk patients**

307 **categorization.** Each of the four main at risk patient categories is represented on the abscissa

308 axis. The respective percentage of each HCW taking care of at-risk patients is expressed on the

309 ordinate axis. The “other” category groups together with children (before 16 years old), pregnant

310 women, patients hospitalized in intensive care unit or severely disabled individuals.

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

312 The HCW agreement to the mandatory influenza vaccination was graduated using a scale from 1

313 (“not at all”) to 10 (“absolutely yes”). Proportions of active HCW categories with a grade

314 corresponded to the X-axis. Physical therapists and nurses were significantly less supportive than

315 physicians and pharmacists ($p < 0.001$), with an important proportion of the active responders

316 (40% and 50% of nurses and physical therapists respectively) giving a “not at all” agreement to

317 mandatory vaccination.

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

319 **cohort.**

320 **Supplementary figures**

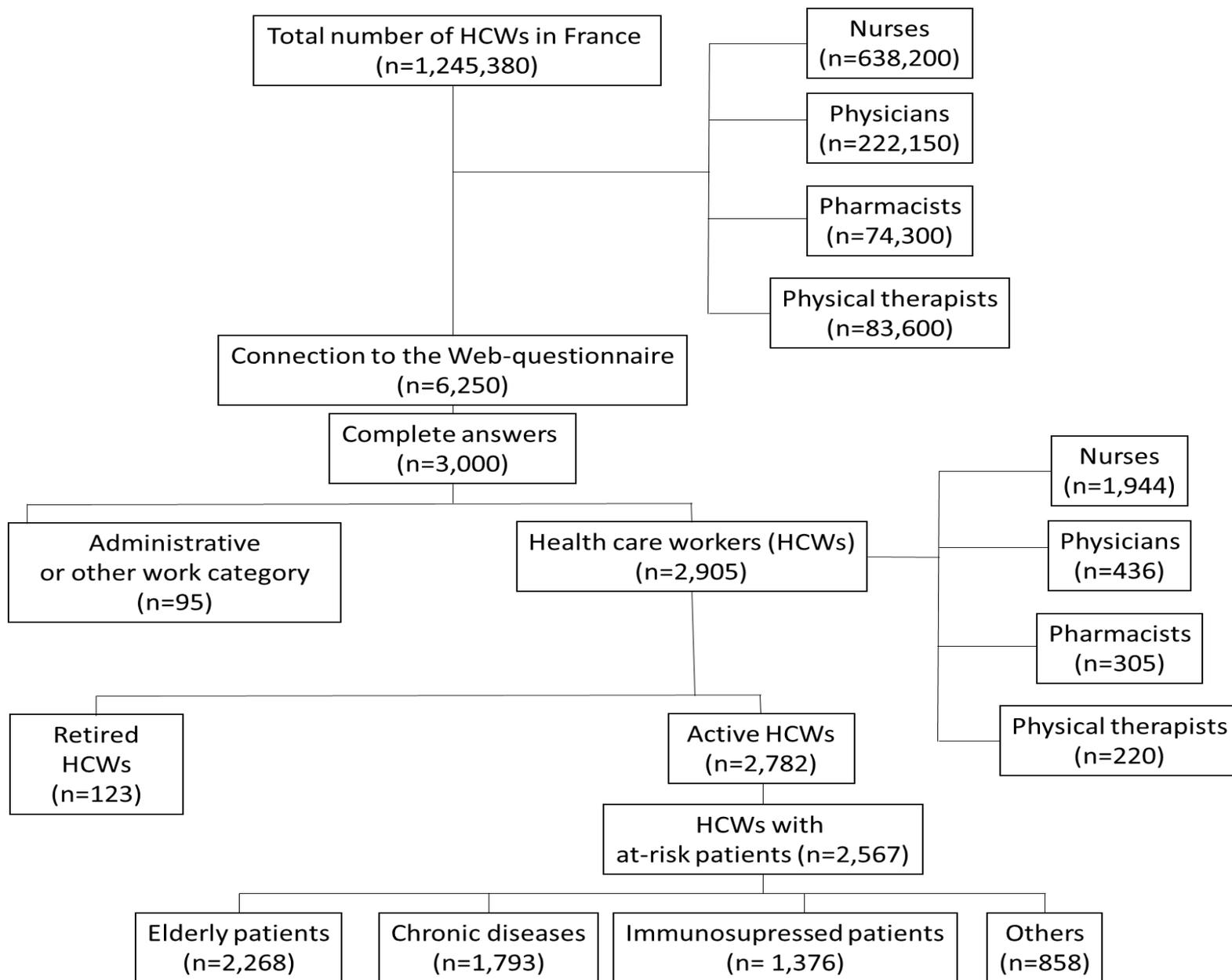
321 **Supplementary figure 1. Electronic questionnaire submitted to the responders.** Each of the
322 14 questions was translated thereafter. 1- Indicate your profession; 2- Are you retired?; 3- What
323 type of patients do you take care of?; 4- Do you work at hospital? ; 5- How do you work (alone or
324 with other HCWs)?; 6-Where do you work?; 7- Are you a man or a woman?; 8-How old are
325 you?; 9- Have you been vaccinated against influenza (epidemiological season 2016-2017)?; 10-
326 When were you vaccinated during this epidemiological season?; 11- Have you already been
327 vaccinated against influenza before?; 12- Will you be vaccinated next year (epidemiological
328 season 2017-2018)?; 13- What do you think of the mandatory vaccination against influenza for
329 HCWs?; 14- Do you think that mandatory vaccination has to be applied solely to HCWs taking
330 care of at-risks patients?

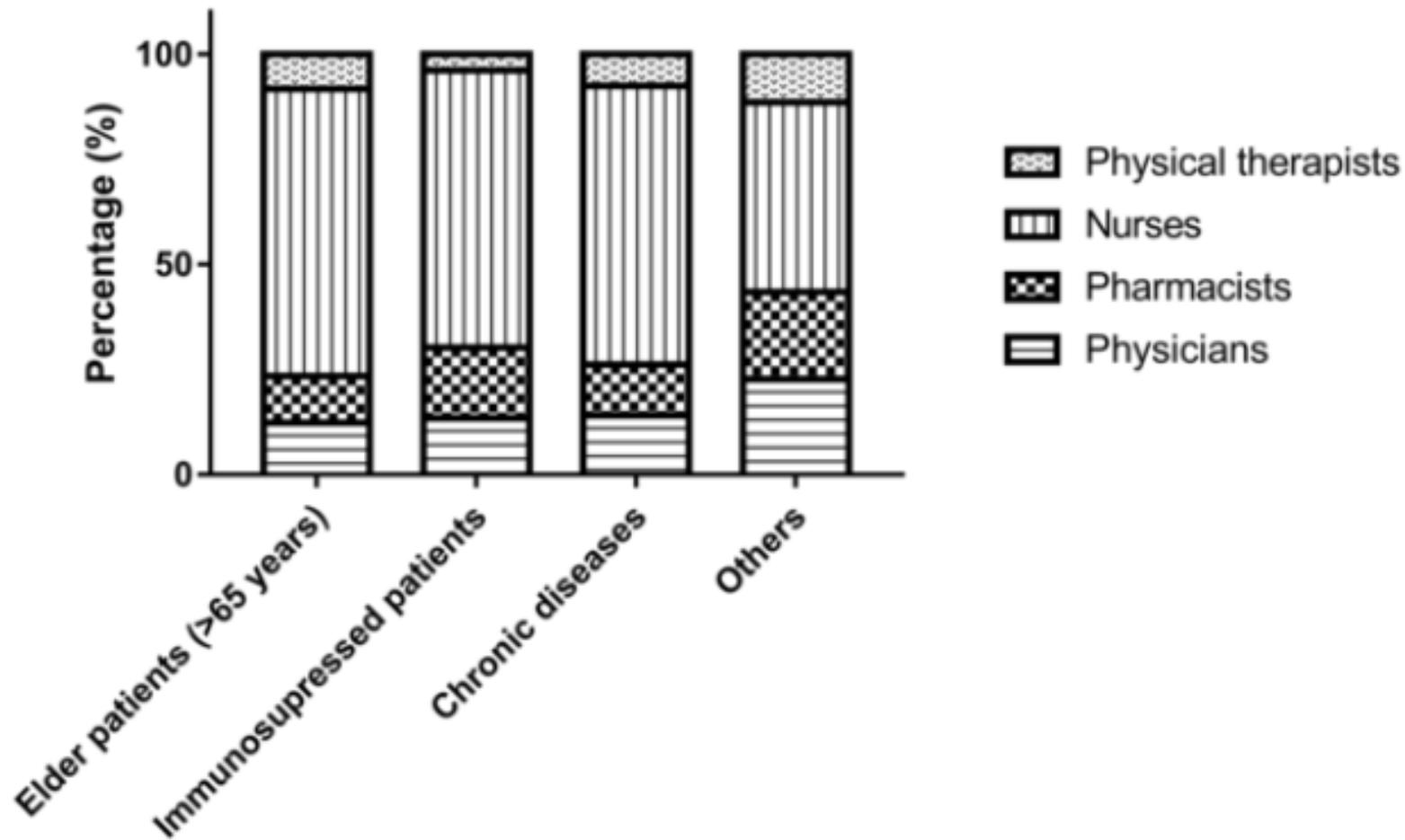
331 **Supplementary figure 2. Age distribution of the responders per HCW category**

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

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

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





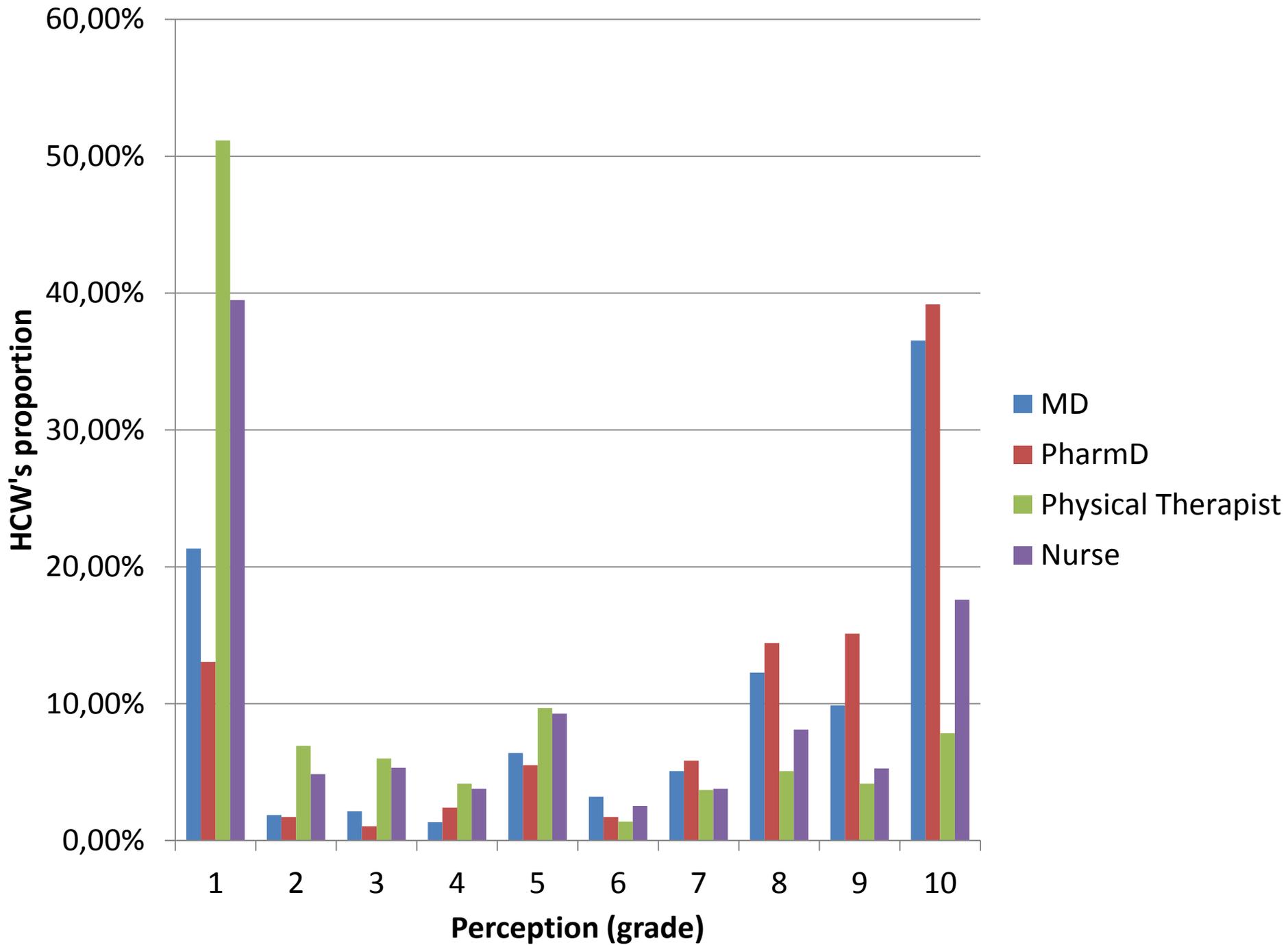


Table 1. Respective proportion of HCW categories, in France and in the responders' cohort.

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]