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## **Acceptability and perception of the herpes zoster vaccine in the 65 and over population: a French observational study**

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## 1 **1. Background**

2 Vaccination is a key determinant for the prevention of infectious diseases whatever the age. It  
3 helps to prolong the working life of seniors and to improve their well-being. Seniors are particularly  
4 vulnerable to infectious diseases such as influenza, pneumonia and herpes zoster (HZ) with a risk of  
5 death for influenza and pneumonia [1,2]. The natural deterioration/alteration of the immune system  
6 caused by ageing results in increased susceptibility to infectious diseases and a decrease in vaccine  
7 efficacy. However, the benefit/risk ratio of the vaccine for a given pathology remains in favor of the  
8 vaccination with a decreased risk of the disease and associated complications [3].

9 In France, vaccination is not mandatory for adults over the age of 65 and influenza vaccination is  
10 only strongly encouraged [4]. A favorable benefit-risk balance has been reported for vaccinations in  
11 this population against influenza, pneumococcal infections, HZ and post-herpetic neuralgia (PHN) [5].  
12 HZ is due to the reactivation of the varicella zoster virus (VZV) which remains latent in the sensory  
13 ganglia following primary infection, i.e. varicella, usually occurring in childhood [6]. It is  
14 characterized by a unilateral eruption that usually develops on the path of a nerve and that affects only  
15 one half of the body on the infected nerve. Affection is sometimes complicated by chronic pain and  
16 disabling PHN [6]. HZ particularly affects older people: the incidence is multiplied by 3 compared  
17 with young adults [7]. In the population above age 70, 30% of the patients with PHN had severe  
18 symptoms for more than one year [7]. Vaccination against HZ is a mean to reduce the burden of this  
19 disease, especially in the elderly and in patients with comorbidities [8]. Since 2015, a vaccine for the  
20 prevention of HZ and PHN is recommended for people aged 65 to 74 years in France [4,9]. It is a live  
21 attenuated vaccine derived from the same strain as that of varicella but has higher antigen content and  
22 administered in a single dose. Its mechanism of action is unprecedented compared with conventional  
23 vaccines since it opposes the reactivation and replication of a virus already present in the organism  
24 (VZV virus contracted in a varicella). Since the vaccine has been put on the market recently, it is  
25 important that the target population have access to this information. Indeed, this vaccine proved its  
26 efficacy in a pivotal randomized clinical trial by reducing the incidence of HZ and PHN by 51% and

27 67% respectively [10]. More recent studies have demonstrated higher vaccine effectiveness against  
28 incident HZ and PHN [11,12].

29 Vaccine acceptance is a driver towards increased vaccine coverage. The aim of this study was  
30 therefore to evaluate acceptability and to describe the perception of vaccination against HZ in a  
31 population of individuals aged 65 living in Lyon, France.

## 32 **2. Methods**

### 33 *2.1. Study design and population*

34 Patients aged 65 and over were asked to participate in our observational study. These patients were  
35 either consulting in one of the thirteen participating private medical biology laboratories or were  
36 hospitalized in the geriatric department or were at the ambulatory medical clinic for a consultation at  
37 Edouard Herriot Hospital, Hospices Civils de Lyon, a public teaching hospital in Lyon, France. To  
38 meet our objective, we decided to perform our study in old people from community and hospital  
39 settings in Lyon area. Recruitment was carried out from January 2018 to March 2019 after receiving  
40 approval from ethics committees. An information form describing the objectives of the study was  
41 given to each patient. After a pilot study in 10 people, a standardized questionnaire (supplementary  
42 data) was administered to patients by a research assistant during a face-to-face interview. Exclusion  
43 criteria included: incomprehension of French and contraindication to receiving HZ vaccine such as  
44 immunosuppressive therapy. Data was collected anonymously.

45 Individuals were interviewed on their knowledge and perceptions of HZ disease and vaccine,  
46 their history of HZ, treatment received and whether they had had PHN. The acceptability of  
47 vaccination was assessed by asking people whether they would agree to be vaccinated against HZ if  
48 they had risk factors. A proven document of vaccine against HZ was requested.

### 49 *2.2. Statistical analysis*

50 Categorical variables were described using percentages. Continuous variables were described  
51 with means and standard deviation (SD). Categorical variables were compared using Fisher or ~~Chi2~~  
52 Chi-square tests and continuous variables were compared using Student or Mann-Whitney tests.

53 Univariate and multivariate logistic regression analyses were performed to detect determinants  
54 associated with patients who would agree to be vaccinated or not. Variables with a p-value <0.1 were  
55 then included in the model for the multivariate analysis. A forward method was used. Variables with a  
56 p-value <0.05 were considered as statistically significant. The risks were expressed as adjusted odds  
57 ratio (aOR) and 95% confidence intervals (CI 95%). Data analysis was performed with R software  
58 (version 3.3.3).

### 59 **3. Results**

60 A total of 907 individuals were interviewed, with a mean age of 75.8 years and a SD of 6.8,  
61 44.7% were males and 59.6% were married or in a relationship and 333 (36.7%) participants had at  
62 least one chronic disease (Table 1). In all, 651 (71.8%) individuals were included from the private  
63 laboratories, 74 (8.2%) from the geriatric department and 182 (20.0%) from the ambulatory care  
64 clinic. Concerning HZ disease, 183 (20.2%) participants had a personal history of HZ, among them,  
65 147 (80.3%) had been treated. A large majority of the individuals (795, 87.6%) knew about HZ and  
66 half of them (51.0%) knew that varicella and HZ viruses were linked. Among the 183 respondents  
67 with a personal history of HZ, 31 (16.9%) had PHN, among them 20 (64.5%) had been treated for  
68 PHN. Concerning vaccination, 761 (83.8%) individuals would agree to be vaccinated (for all vaccines)  
69 and 625 (68.9%) would agree to be vaccinated against HZ if they had risk factors. A total of 108  
70 (11.9%) individuals were aware of vaccine recommendations and 46 (5.1%) were aware of the  
71 recommendations for HZ vaccine. Finally, 814 (89.7%) participants thought that vaccination was a  
72 good prevention tool, while only 483 (53.3%) thought that vaccination was a good prevention tool  
73 against HZ (Table 2).

#### 74 *3.1. Vaccination acceptability*

75 Patients with HZ risk factors, who did not agree to be vaccinated against HZ were significantly older  
76 (76.9 vs 75.3 years, p=0.009) and the percentage of females was higher (Table 3). The percentage of  
77 hospital patients (geriatric care department or ambulatory medical-clinic) was significantly higher  
78 (36.2% vs 24.6% in the other group, p<0.001). The percentage of people who thought that HZ was  
79 always severe (64.2% vs 52.8%, p=0.002) was significantly higher in the group who would agree to be

80 vaccinated against HZ. The proportion of participants who thought that vaccination was a good  
81 prevention tool against HZ (64.8% vs 27.8%,  $p<0.001$ ), who would agree to be vaccinated for all  
82 vaccines (94.4% vs 60.3%,  $p<0.001$ ) and who thought that vaccination was a good prevention tool  
83 (93.8% vs 80.9%,  $p<0.001$ ) was also statistically significantly higher in the group of people who  
84 would agree to be vaccinated against HZ if they had risk factors compared with those who would not  
85 agree to be vaccinated. The variables significantly associated with the agreement of being vaccinated  
86 against HZ were (Table 4): participants who would agree to be vaccinated against any infectious  
87 diseases were more likely to be vaccinated against HZ (aOR = 10.9, 95%CI 7.1-17.3). Individuals  
88 enrolled from private laboratories (aOR =2.7, 95%CI 1.7-4.5), male (aOR = 1.5, 95%CI 1.1 – 2.2) and  
89 individuals who thought that vaccination is a good prevention tool (aOR = 1.7, 95%CI 1.0-2.9) were  
90 more likely to be vaccinated against HZ if they are at risk.

#### 91 **4. Discussion**

92 The aim of this observational study was to evaluate acceptability and perception of HZ vaccination in  
93 a group of >65 year-old population in Lyon, France. The acceptability of vaccination seemed  
94 satisfactory with 625 (68.9%) participants would agree to be vaccinated if they had risk factors,  
95 suggesting that better information could improve vaccination coverage.

96 The vaccine is effective, safe and well tolerated. Effectiveness studies conducted in several countries  
97 yielded results consistent with those obtained in randomized and controlled clinical trials, and  
98 confirmed the good safety and tolerability profiles of the vaccine, as well as its good  
99 efficacy/effectiveness against HZ and PHN in participants >60 years of age [14]. In France, the  
100 vaccine has been recommended since 2015. However, despite the benefits of vaccination, less than 2%  
101 of the target population was vaccinated [13].

102 .HZ as a disease is better known by participants, in the community as in hospital, than the vaccine  
103 against HZ. As expected, only 92 (10%) respondents were aware of the availability of the HZ vaccine  
104 which is similar to the study by Valente et al. [14]. A quarter of the individuals reported a history of  
105 HZ and two-thirds (64%) knew someone with a history of HZ. Thirty-one individuals (17%) reported  
106 an alteration in their daily quality of life caused by post-zoster pain which is fewer than previous

107 studies [7]. This pathology is often accompanied by severe pain and can lead to chronic functional  
108 consequences with a significant impact on functional autonomy [15]. Five hundred and fifty (61%)  
109 respondents described HZ disease as always severe. Similarly, Valente et al. reported that 47% of  
110 respondents rated HZ associated pain as "severe" and 39% "moderate" [14].

111 The lack of or low patient awareness, and lack of or insufficient advice from physicians were  
112 reported as main barriers for vaccination [14]. Our results highlighted the vital role of physicians to  
113 play in promoting vaccination. Likewise, knowing someone who had had HZ seemed to increase  
114 willingness to have the vaccine, presumably due to a greater awareness of the disease and its  
115 consequences, although this not reached statistical significance as in other study [14].

116 Our results showed that being in favourable of vaccinations in general have a strong influence on  
117 vaccination acceptability which can be explained by the self-confidence of people already pro-  
118 vaccinations and who are not worried about possible side effects when the goal is health protection.

119 In this study we addressed some barriers which are one of the modifying variables of the Health  
120 Belief Model [16]. Further studies need to more deeply explore the perceived threats and cues to  
121 action to improve HZ vaccine acceptability and uptake.

122 One strength of this prospective study was to document the perception of the HZ vaccine at an  
123 early stage of its "life" in a large sample of old people living in Lyon, France. This survey provided  
124 information and reinforced vaccination prevention added-value among three groups of old people  
125 assumed to be medically followed. The geographical representation of the laboratories is satisfactory  
126 because they cover the Lyon metropolitan area (800,000 inhabitants).

127 A selection bias may exist because the interviewees were not representative of the general population.  
128 On one hand, the majority of participants were recruited from private laboratories. They were more  
129 health conscious and therefore were more able to be informed and vaccinated, which might have  
130 overestimated knowledge about HZ vaccine. On the other hand, participants were recruited in geriatric  
131 department, population who differs from the HZ vaccine's target population, which might have biased  
132 the representativeness of the results. Additionally, collected responses might have been partially  
133 influenced by recall bias, especially considering the age of the respondents. Even though, the  
134 questionnaire was administered by trained research assistant in order to minimize this source of error.

135 **5. Conclusion**

136 In conclusion, participants had prior knowledge of HZ. However, they were not aware of the  
137 existence of a vaccine. Physicians should remain supportive of vaccination and seek to convince their  
138 hesitant patients.

139 To our knowledge, this is the first study in France that aimed to inform a target population of the  
140 availability of the HZ vaccine recommended for immunocompetent patients from 65 to 74 years of  
141 age. The access to vaccine information is a challenge among the general population. Our study showed  
142 that in people known the existence HZ, the information was get from media. Then, an information  
143 campaign using such commodities could be a good way in the target population to raise awareness.  
144 Community pharmacists and general practitioners may play a key role in informing the target  
145 population about the availability of the vaccine against HZ specifically in patients with greater risk of  
146 HZ [17].

147 Better immunization coverage in this age group will ultimately contribute to the better well-being  
148 of these individuals by preserving functional abilities, pain reduction and avoiding loss of vision in  
149 case of ocular complications [18].

150 This study reports that lack of knowledge is a major issue regarding prevention by vaccines  
151 including their beneficial consequences. Vaccine hesitancy, as defined by the WHO as the delay of  
152 refusal of vaccines despite their availability, is a major challenge. Addressing this issue and its  
153 determinants is complex but essential to increase HZ vaccine coverage.



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159 **Conflicts of Interest related to this study**

160 The authors declare no conflict of interest

161 **Ethics committees**

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205 **Table 1:** Characteristics of seniors (>65 years old) included in the study between January 2018 and  
 206 March 2019

	Private laboratory N=651	Ambulatory medical clinic N=182	Geriatric department N=74	Total N=907	P
<b>Characteristics of enrolled patients</b>					
Mean age (years) ± SD	75.8 ± 6.8	73. ±6.5	86.7 ±5.3	75.7 ±7.4	<0.001
Gender:					0.013
- Males	310 (47.6)	70 (38.5)	25 (33.8)	405 (44.7)	
- Females	341 (52.4)	112 (61.5)	49 (66.2)	502 (55.3)	
Marital status:					<0.001
- In a relationship/married	400 (61.4)	121 (66.5)	20 (27.0)	541 (59.6)	
- Single	251 (38.6)	61 (33.5)	54 (73)	366 (40.4)	
Education level:					0.02
- Primary/secondary school	343 (52.7)	104 (57.1)	48 (64.9)	499 (55.0)	
- High school	136 (20.9)	46 (25.3)	16 (21.6)	198 (21.8)	
- University	172 (26.4)	32 (17.6)	10 (13.5)	210 (23.2)	
Underlying chronic diseases	217 (33.3)	90 (49.4)	26 (35.1)	333 (36.7)	<0.001
<b>Knowledge of varicella and Herpes zoster (HZ)</b>					
Personal history of HZ	140 (21.5)	36 (19.7)	7 (9.4)	183 (20.2)	0.07
Treatment of HZ	114/140 (81.4)	30/36 (83.3)	3/7 (42.8)	147/183 (80.3)	0.07
People who know HZ	571 (87.7)	167 (91.7)	57 (77)	795 (87.7)	0.07
People who know that varicella and HZ are linked	337 (51.7)	101 (55.4)	25 (33.7)	463 (51.0)	0.03
Personal history of varicella	424 (65.1)	137 (75.2)	45 (60.8)	606 (66.8)	0.06
People who think that HZ causes pain	533 (81.8)	147 (80.7)	45 (60.8)	725 (80.0)	<0.001
Pain type as supposed in patients who think that HZ is painful					<0.001
- Acute pain	262 (49.2)	83 (56.5)	15 (33.3)	360 (49.7)	
- Chronic pain	62 (11.6)	14 (9.5)	5 (11.1)	81 (11.2)	
- Acute and chronic pain	135 (25.3)	25 (17.0)	7 (15.6)	167 (23.0)	
- Burns and itching	55 (10.3)	21 (14.3)	6 (13.3)	82 (11.3)	
- Do not know	19 (3.6)	4 (2.7)	12 (26.7)	35 (4.8)	

208 **Table 2:** Acceptability and perception of the herpes zoster in patients included in the study between  
 209 January 2018 and March 2019

	Private laboratory N=651 (%)	Ambulatory medical clinic N=182 (%)	Geriatric department N=74 (%)	Total N=907 (%)	P
People who know someone with a history of HZ	423 (64.9)	120 (65.9)	39 (52.7)	582 (64.2)	0.12
<b>Complications of HZ</b>					
Personal history of post-herpetic neuralgia (PHN)	26/140 (18.5)	4/36 (11.1)	1/7 (14.2)	31/183 (16.9)	0.93
Treatment of PHN	17/26 (65.3)	3/4 (75)	0/1 (0)	20/31 (64.5)	0.36
Impairment in activities of daily life due to PHN	11/26 (42.3)	2/4 (50)	1/1 (100)	14/31 (45.2)	0.87
People who think HZ is always severe	408 (62.6)	114 (62.6)	28 (37.8)	550/907 (60.6)	<0.001
<b>HZ Vaccine</b>					
People who know that a vaccine exists	71 (10.9)	13 (7.1)	8 (10.8)	92 (10.1)	0.05
Source of information in people who are aware of the existence of HZ vaccine					0.003
Media	43 (60.6)	8 (61.5)	3 (37.5)	54 (58.7)	
GP	15 (21.1)	3 (23.1)	3 (37.5)	21 (22.8)	
Friends/family	8 (11.3)	2 (15.4)	1 (12.5)	11 (12.0)	
Social network	1 (1.4)	0 (0)	1 (12.5)	2 (2.2)	
Other	0 (0)	0 (0)	1 (12.5)	1 (1.1)	
People who know the recommendations (people aged 65-74 years old)	30 (42.3)	7 (53.8)	2 (25)	39 (42.4)	0.43
People who agree to be vaccinated against HZ if they have risk factors	471 (72.3)	119 (65.3)	35 (47.2)	625 (68.9)	<0.001
People who think vaccination is a good prevention tool against HZ	342 (52.5)	103 (56.5)	38 (51.3)	483 (53.3)	0.91
People vaccinated against HZ	3 (0.4)	0 (0)	0 (0)	3 (0.3)	0.55

210 GP: General practitioner.

211 **Table 3:** Determinants associated with agreement or not to be vaccinated against HZ in case of risk  
 212 factors in included patients between January 2018 and March 2019

Variables	Agree N=625 (%)	Do not agree N=282 (%)	p-value
Mean age (years)	75.2	76.9	0.06
Marital status			< 0.001
- In a relationship/married	404 (64.6)	137 (48.6)	
- Single	221 (35.4)	145 (51.4)	
Gender:			< 0.001
- Male	310 (49.6)	95 (33.7)	
- Female	315 (50.4)	187 (66.3)	
Education level:			0.22
- Primary/secondary school	329 (52.6)	166 (58.9)	
- High school	142 (22.7)	74 (26.2)	
- University	154 (24.7)	60 (21.3)	
Underlying chronic diseases	238 (38.1)	95 (33.7)	0.21
Origin			< 0.001
- Private laboratory	471 (75.4)	180 (63.8)	
- Geriatric care department	35 (5.6)	39 (13.8)	
- Ambulatory medical clinic	119 (19.0)	63 (22.4)	
Personal history of HZ	122 (19.5)	61 (21.6)	0.48
Treatment of HZ	95/122 (77.9)	52/61 (85.2)	0.32
People who know someone with a history of HZ	406 (65.0)	176 (62.4)	0.50
People who think HZ causes pain	512 (81.9)	213 (75.5)	0.03
People who think HZ is always severe	401 (64.2)	149 (52.8)	0.002
Personal history of PHN	18/122 (14.8)	13/61 (21.3)	0.30
Treatment of PHN	12/18 (66.7)	8/13 (61.5)	0.99
Impairment in activities of daily living due to PHN	9/18 (50)	5/13 (38.5)	0.72
People who know HZ vaccine	65 (10.4)	27 (9.6)	0.81
People who think vaccination is a good prevention tool against HZ	405 (64.8)	78 (27.8)	< 0.001
People who agree to be vaccinated (all vaccines)	590 (94.4)	170 (60.3)	< 0.001

214 **Table 4:** Determinants associated with agreement or not to be vaccinated against HZ in case of risk  
 215 factors, Lyon, 01/2018-03/2019, multivariate analysis

Variable	aOR*	CI95%	p-value
People who agree to be vaccinated (all vaccines)	10.9	7.1-17.3	< 0.001
Origin:			0.003
- Geriatric care department	1.0		
- Private laboratory	2.7	1.7-4.5	
- Ambulatory medical clinic	2.1	1.2-3.6	
Sex:			0.01
- Female	1.0		
- Male	1.5	1.1-2.2	
People who think vaccination is a good prevention tool	1.7	1.0-2.9	0.048

216 aOR\*: adjusted odds-ratio.