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Original Article

Vaccine Hesitancy Among General Practitioners and Its Determinants During Controversies: A National Cross-sectional Survey in France

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ABSTRACT

Background: This study aimed to assess: 1) vaccine hesitancy (VH) prevalence among French general practitioners (GPs) through the frequency of their vaccine recommendations, and 2) the determinants of these recommendations.
Methods: Cross-sectional observational study in 2014 nested in a national panel of 1712 randomly selected GPs in private practice in France. We constructed a score of self-reported recommendation frequency for 6 specific vaccines to target populations.
Results: 16% to 43% of GPs sometimes or never recommended at least one specific vaccine to their target patients. Multivariable logistic regressions of the dichotomized score showed that GPs recommended vaccines frequently when they felt comfortable explaining their benefits and risks to patients (OR = 1.87; 1.35–2.59), or trusted official sources of information highly (OR = 1.40; 1.01–1.93). They recommended vaccines infrequently when they considered that adverse effects were likely (OR = 0.71; 0.52–0.96) or doubted the vaccine's utility (OR = 0.21; 0.15–0.29).
Interpretation: Our findings show that after repeated vaccine controversies in France, some VH exists among French GPs, whose recommendation behaviors depend on their trust in authorities, their perception of the utility and risks of vaccines, and their comfort in explaining them. Further research is needed to confirm these results among health care workers in other countries.

1. Introduction

Over the past two decades several vaccine controversies have emerged in various countries, including France, inducing worries about severe adverse effects and eroding confidence in health authorities, experts, and science (Larson et al., 2011). These two dimensions are at the core of the vaccine hesitancy (VH) observed in the general population. VH is defined as delay in acceptance of vaccination, or refusal, or even acceptance with doubts about its safety and benefits, with all these behaviors and attitudes varying according to context, vaccine, and personal profile, despite the availability of vaccine services (SAGE Group 2014) (Larson et al., 2014; Dubé et al., 2013). VH presents a challenge to physicians who must address their patients' concerns about vaccines and ensure satisfactory vaccination coverage.

Physicians, and especially general practitioners (GPs), are the cornerstone of vaccination implementation in most countries and their recommendations play an influential role in their patients' vaccine behavior (Gust et al., 2008; Freed et al., 2011; Schwarzinger et al., 2010). In France, GPs write prescriptions for 90% of the vaccinations purchased. Patients may return to the GP for administration after purchasing the vaccine, but they may also see a nurse or make other arrangements or fail to follow up (Ecole des Hautes Etudes en Santé Publique, 2013). Although physicians are generally favorable to vaccination, some, especially those whose practice includes but is not limited to homeopathy or acupuncture, are known to be negative toward vaccination in general or toward some particular vaccines (Benin et al., 2006; Pulcini et al., 2013;

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François et al., 2011). Moreover, the percentage of physicians reporting doubts about the harmlessness of vaccines is growing (Dubé et al., 2013). Physicians may therefore share some of the same questions and concerns expressed by the general population (Poland, 2010) and distrust health authorities, just as the population does (Yaqub et al., 2014). These findings raise the question of whether doubts about vaccine safety and distrust of the health authorities might fuel VH among physicians. Vaccine-hesitant physicians are likely to recommend vaccines to their patients at lower rates and with less conviction than nonhesitant physicians (Dubé et al., 2013; Bean and Catania, 2013).

As part of a national panel of 1712 GPs in private practice in France, we conducted a study of this topic with two main objectives. First, we sought to assess the presence, extent, and variability of VH among French GPs, in relation to six vaccine situations (specific vaccine and target population) with suboptimal vaccination coverage: we assessed their VH through their self-reported recommendation behavior. Second, we sought to test factors associated with GPs' vaccine recommendations, after verifying that their recommendations were correlated to their own vaccination behavior. Several specific vaccines are or have been controversial in France: questions have been raised about the safety and benefits of vaccines against hepatitis B, HPV and seasonal influenza, as well as against adjuvants (Appendix, Table A1), and about the reliability of the information disseminated by health authorities about them. Other vaccines remain uncontroversial, including MMR (perhaps surprisingly) and the vaccine against meningococcal meningitis C. We expected that GPs' beliefs about vaccine utility in general and their self-efficacy — beliefs in their ability to convince patients to be vaccinated (Bandura, 1994) — would be positively correlated to their recommendation of all vaccines, either controversial or not (hypothesis 1). On the other hand, we also expected that GPs' beliefs about vaccine safety and trust in health authorities would be negatively correlated to their recommendations for controversial, but not for uncontroversial, vaccines (hypothesis 2).

2. Methods

2.1. Population

The panel was designed to collect data regularly about GPs' medical practices, working conditions, and opinions about public health regulatory policies and was set up following the methods used for a previous panel (Verger et al., 2012). Enrolment took place between November 2013 and March 2014: we selected GPs in private practice (non-salaried) by random sampling from the Ministry of Health's exhaustive database of health professionals in France ("Répertoire Partagé des Professionnels de Santé"). Sampling was stratified for sex, age (tertiles in the sampling base: <50, 50–58, >58 years), and annual number of office consultations and house calls (workload), obtained from the exhaustive reimbursement database of the National Health Insurance Fund for each GP in 2012. Sampling was also stratified for the density of each GP's municipality of practice. The sample size was set so that the smallest stratum resulting contained at least 10 GPs. Agreement to participate in the panel meant agreeing to respond to a cross-sectional survey every six months for two and a half years. GPs planning to retire within 6 months or who practiced acupuncture or homeopathy or other alternative medicine exclusively were excluded. To limit any selection bias that might have resulted from particular opinions or attitudes, the specific topics to be studied were not mentioned to GPs before they were asked to participate. The National Authority for Statistical Information (Commission Nationale de l'Information Statistique) approved the panel.

The first cross-sectional survey in this panel focused on vaccination behaviors and attitudes and took place from April to July 2014. GPs received a compensation equivalent to one consultation fee for their participation in this survey.

2.2. Procedure and Questionnaires

Professional investigators first contacted GPs to ask them to participate, obtain their consent, and verify inclusion criteria; they then conducted the inclusion interview, with computer-assisted telephone interview (CATI) software. The interview included a short standardized questionnaire collecting information about participants' professional characteristics (Table 1). In the second step, participants received written consent forms to return to us.

We developed a standardized questionnaire for the first cross-sectional interview after reviewing the literature, conducting qualitative interviews on the topic with 10 GPs, and discussing it with experts. We pilot-tested the questionnaire for clarity, length, and face validity among 50 GPs and modified several questions found to be unclear.

As summarized in Table 2, the questionnaire collected information about: 1) the frequency at which GPs recommended vaccines in six specific situations, chosen because their current coverage in France does not meet official objectives; 2) GPs' opinions about the likelihood of links between potential severe adverse effects and certain vaccines or vaccine components (adjuvants) that have been or still are the subject of public and/or scientific debate in France or elsewhere (six items); 3) GPs' beliefs about the utility of vaccines; 4) GPs' confidence in their

Table 1
Social, demographic, and professional characteristics of the study population (French nationwide panel of general practitioners, unweighted data).

No. (%)	Refusals (n = 2012)	Panel participants (n = 1712)[a]	Survey participants (n = 1582)
Stratification variables			
Gender			
Male	1482 (73.7)	1100 (64.3[b])	1014 (64.1)
Female	530 (26.3)	612 (35.7)	568 (35.9)
Age — years			
<50	559 (27.8)	618 (36.1[b])	580 (36.7)
50–58	732 (36.4)	622 (36.3)	573 (36.2)
>58	721 (35.8)	472 (27.6)	429 (27.1)
GPs density of the municipality of practice			
<− 19.3% of national average	601 (29.9)	511 (29.8)	474 (30.0)
Between − 19.3% and + 17.7% of national average	957 (47.5)	818 (47.8)	753 (47.6)
>+17.7% of national average	454 (22.6)	383 (22.4)	355 (22.4)
2012 workload			
<3067 procedures	369 (18.3)	349 (20.4[c])	318 (20.1)
3067–6028 procedures	953 (47.4)	854 (49.9)	793 (50.1)
>6028 procedures	690 (34.3)	509 (29.7)	471 (29.8)
Practice population characteristics[d]			
Proportion of patients aged under 16 (%)			
[0–16]	–	371 (23.9)	333 (23.3)
[17–21]	–	387 (24.9)	353 (24.7)
[22–25]	–	402 (25.9)	380 (26.6)
[26–50]	–	393 (25.3)	364 (25.5)
Proportion of patients aged over 70 (%)			
[0–8]	–	459 (29.6)	422 (29.5)
[9–12]	–	391 (25.2)	361 (25.2)
[13–17]	–	361 (23.3)	335 (23.4)
[18–67]	–	342 (22.0)	312 (21.8)
Professional characteristics			
Practice			
Group	–	1002 (58.5)	929 (58.7)
Solo	–	710 (41.5)	653 (41.3)
Occasional practice of alternative medicine[e]			
No	–	1511 (88.3)	1403 (88.7)
Yes	–	201 (11.7)	179 (11.3)

[a] Chi-square test: refusals vs participants in the panel.
[b] $P \leq .001$.
[c] $P \leq .05$.
[d] Quartiles; 159 missing values.
[e] Alternative medicine: homeopathy and/or acupuncture.

Table 2
Practices, opinions, and attitudes of GPs regarding vaccination (weighted data, N = 1582).

Frequency of vaccine recommendations (line %)	Never	Sometimes	Often	Always
MMR to non-immune adolescents and young adults	4.3	12.9	22.9	59.9
Meningococcal meningitis C to ages 2–24 (catch-up)[a]	17.6	25.7	23.4	33.3
Meningococcal meningitis C to 12-month-old infants	15.7	16.7	15.9	51.7
Human papilloma virus vaccine to girls aged 11–14[b]	10.5	17.2	26.8	45.6
Hepatitis B to adolescents (catch-up)	10.9	26.0	29.1	34.0
Seasonal influenza to adults under 65 with diabetes	4.5	11.6	26.2	57.6
Trust in the reliability of information provided by official sources about vaccination (line %)	No trust	Distrust somewhat	Somewhat trust	Strong trust
Ministry of Health[b]	5.7	13.3	55.1	25.9
Public health agencies	2.8	8.8	57.1	31.3
Scientific sources	1.7	3.6	48.3	46.4
Specialist colleagues	3.4	5.4	52.0	39.3
Perceived likelihood of links between specific vaccines and potential severe adverse effects (line %)	Not at all likely	Not very likely	Somewhat likely	Very likely
Seasonal influenza vaccine & Guillain–Barré syndrome[a]	21.5	54.2	20.5	3.8
Hepatitis B vaccine & multiple sclerosis	48.1	40.3	9.2	2.5
Aluminum adjuvants & Alzheimer's disease	38.4	50.0	8.7	2.9
AS03-adjuvanted 2009 A/H1N1 vaccine (Pandemrix) & narcolepsy[a]	29.7	49.1	16.5	4.8
Human papilloma vaccine & multiple sclerosis	51.3	43.3	4.5	0.9
Vaccines containing adjuvant & long-term complications	18.4	48.8	26.3	6.5
Perceptions of vaccines utility (line %)	Strongly disagree	Somewhat disagree	Somewhat agree	Strongly agree
Today some vaccines recommended by authorities are not useful[b]	38.3	35.3	20.0	6.4
Children are vaccinated against too many diseases[b]	53.1	26.7	14.6	5.5
Self-efficacy: confidence in one's ability to explain vaccines (line %)	Very unconfident	Somewhat unconfident	Somewhat confident	Very confident
Vaccine utility	0.9	2.9	41.7	54.5
Vaccine safety[a]	2.2	15.8	55.7	26.2
Role of adjuvants	11.1	45.7	32.2	11.0

Abbreviations: MMR, measles, mumps and rubella.
[a] One missing value.
[b] Two missing values.

ability to explain the benefits and risks of vaccines and the role of adjuvants to their patients (as a proxy for self-efficacy in explaining vaccination to patients); and 5) GPs' trust in the reliability of various sources of information about vaccine benefits and risks. For all of these items, we collected answers with 5-point Likert scales that included a "no opinion" answer.

In addition, participants were asked about their own vaccinations (2013–2014 seasonal influenza and hepatitis B), whether they had had any patients in the past five years with any of the following vaccine-preventable diseases (VPDs): measles, acute or recently diagnosed chronic hepatitis B, bacterial meningitis, cervical cancer, or a hospital admission for a complication of seasonal influenza. Finally, they were asked if they had attended any continuous medical education (CME) courses on infectious diseases and vaccination in the previous year.

2.3. Statistical Analysis

To match the sample more closely to the national French GP population for the stratification variables, we weighted the data with SURVEY procedures (PROC SURVEYFREQ, PROC SURVEYLOGISTIC, SAS 9.4 statistical software).

We constructed two dependent variables by summing GPs' responses on the Likert scales to the corresponding items to calculate: a global score of the reported frequency of their vaccine recommendations to patients ("global score of vaccine recommendations"; six items; the lower the score the most likely they were to be vaccine-hesitant); and a subscore for the frequency of their recommendations of vaccines that are not controversial in France (MMR, meningococcal meningitis C in infants and in young adults; three items); we dichotomized these two scores at the median.

Finally, we constructed four explanatory variables of interest: one summing GPs' opinion of the likelihood of specific potential severe adverse effects for each of six vaccines ("perceived vaccine adverse effects", six items); a score of "doubts about vaccine utility" (two items); a proxy score for GPs' self-efficacy regarding their ability to explain the benefits and risks of vaccines to their patients ("self-efficacy", three items); and a score of GPs' trust in the reliability of information provided by official sources about these benefits and risks ("trust in official sources", four items). We categorized these four explanatory variables by their quartiles.

For all six scores (the two dependent and four explanatory variables), we calculated Cronbach's alpha coefficients to measure their internal consistency (Bland and Altman, 1997; Tavakol and Dennick, 2011): Internal consistency was considered satisfactory at values of $0.7 < \text{alpha} < 0.8$ and acceptable at values of $0.6 < \text{alpha} < 0.7$ (Table A2, Appendix). Principal component analyses confirmed the unidimensionality of each score (Table A2, Appendix).

We used a multivariable logistic regression adjusted for the stratification variables to test the association between the dichotomized global score of vaccine recommendations and GPs' own vaccinations (2013–2014), seasonal influenza (yes or no), hepatitis B (3 doses or more or fewer than 3 doses or none). We also used multivariable logistic regressions to test associations between the two dependent variables and the four variables of interest, adjusting the models for the stratification variables, GPs' professional characteristics, and the number of different vaccine-preventable diseases in the practice (Table 3).

We computed the variance inflation factor (VIF) to test for multicollinearity in equivalent linear models and interpreted VIF values <5 as presenting no multicollinearity issues (Rogerson, 2001). To test

Table 3
Factors associated with vaccine recommendations[a] by GPs (logistic regressions, weighted data, N = 1572[b]).

Explanatory variables	Global score (ref. <19)		Subscore for uncontroversial vaccines (ref. <9)	
	Univariable regression	Multivariable regression	Univariable regression	Multivariable regression
	ORa [95% CI]			
Stratification variables				
Gender (ref. male)				
Female	1.38 [1.13;1.68]	1.53 [1.19;1.96]	1.69 [1.37;2.09]	1.73 [1.33;2.26]
Age, years (ref. <50)				
50–58	0.68 [0.55;0.86]	0.79 [0.61;1.03]	0.51 [0.40;0.65]	0.57 [0.43;0.76]
>58	0.52 [0.41;0.66]	0.64 [0.48;0.86]	0.34 [0.26;0.43]	0.41 [0.30;0.55]
2012 workload (ref. <3067 procedures)				
3067–6028 procedures	1.98 [1.54;2.55]	1.56 [1.17;2.07]	1.78 [1.39;2.28]	1.42 [1.05;1.92]
>6028 procedures	2.18 [1.64;2.89]	1.81 [1.30;2.52]	2.04 [1.54;2.71]	1.86 [1.31;2.64]
GPs density of municipality of practice (ref. <— 19.3% of the national average)				
Between −19.3% and +17.7% of the national average	0.99 [0.79;1.24]	0.89 [0.69;1.15]	1.18 [0.93;1.48]	1.11 [0.85;1.44]
>+17.7% of the national average	0.88 [0.67;1.14]	0.86 [0.63;1.16]	1.02 [0.78;1.33]	1.03 [0.75;1.41]
Professional characteristics				
Occasional practice of alternative medicine[c] (ref. no)				
Yes	0.27 [0.19;0.37]	0.47 [0.33;0.67]	0.30 [0.22;0.41]	0.52 [0.37;0.73]
CME on infectious diseases and vaccination in 2013 (ref. no)				
Yes	1.56 [1.28;1.90]	1.24 [1.00;1.55]	1.56 [1.27;1.92]	1.23 [0.97;1.55]
Number of different VPDs among GPs' patients [0–5]	0.79 [0.73;0.86]	1.12 [1.01;1.23]	0.81 [0.74;0.88]	1.05 [0.96;1.16]
Confidence scores[d]				
Self-efficacy: confidence in one's ability to explain vaccines (ref. low ([3;7]))				
Medium ([8;9])	1.94 [1.47;2.55]	1.45 [1.08;1.96]	1.75 [1.33;2.30]	1.37 [1.01;1.86]
High ([10;12])	2.70 [2.02;3.61]	1.87 [1.35;2.59]	2.02 [1.51;2.70]	1.50 [1.07;2.09]
Trust in official sources about vaccination (ref. low ([4;11]))				
Medium ([12;13])	1.89 [1.44;2.49]	1.20 [0.88;1.63]	1.89 [1.44;2.47]	1.16 [0.86;1.59]
High ([14;16])	3.04 [2.28;4.04]	1.40 [1.01;1.93]	2.98 [2.24;3.98]	1.35 [0.96;1.89]
Scores of perception of vaccine risk and utility[d]				
Perception of potential severe adverse effects (ref. low ([6;9]))				
Medium ([10;12])	0.66 [0.51;0.85]	0.74 [0.56;0.99]	0.71 [0.54;0.94]	0.76 [0.56;1.03]
High ([13;24])	0.38 [0.29;0.49]	0.71 [0.52;0.96]	0.42 [0.32;0.55]	0.77 [0.55;1.07]
Doubts about vaccine utility (ref. low (2))				
Medium ([3;4])	0.57 [0.44;0.73]	0.66 [0.51;0.86]	0.54 [0.41;0.71]	0.59 [0.44;0.80]
High ([5;8])	0.13 [0.09;0.17]	0.21 [0.15;0.29]	0.13 [0.10;0.18]	0.20 [0.14;0.28]
Nagelkerke R^2		0.25		0.26

Abbreviations: ORa, adjusted odds-ratio; CI, confidence interval; CME, continuing medical education; VPD, vaccine-preventable disease.
Self-efficacy: the higher the score, the more self-efficacious GPs feel about their ability to explain the benefits and risks of vaccines to their patients.
Trust in official sources about vaccination: the higher the score, the more trust GPs have in the reliability of information provided by official sources about vaccines' benefits and risks.
Perception of potential severe adverse effects: the higher the score, the more GPs consider that links between six vaccines and specific potential severe adverse effects are likely.
Doubts about vaccine utility: the higher the score, the greater the doubts GPs express about vaccine utility.

[a] Both scores dichotomized at the median.
[b] 10 missing values.
[c] Homeopathy and/or acupuncture.
[d] All scores constructed by summing the responses to the Likert scales of the corresponding items (see Table 2 for details); they were then categorized according to quartiles (Q1, Q2–3, Q4).

whether the differences between panel participants and non-participants might have biased the estimations of the regression analyses, we implemented a bivariate probit model with sample selection (which makes it possible to test for the presence of selection bias and to correct it, see the Appendix for a further explanation of this model) (Heckman, 1979; Greene, 2003; Obrizan, 2010). The likelihood-ratio (LR) test of independent equations was used to test the null hypothesis of no correlation between error terms from each equation. Finally, to verify the robustness of our results, we conducted sensitivity analyses with a dichotomization threshold at the mean + 1 standard deviation for the vaccine recommendation scores.

All analyses were based on two-sided *P*-values, with statistical significance defined by $P \leq 0.05$. They were conducted with SAS 9.4 statistical software (SAS Institute, Cary, NC).

2.4. Funding

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3. Results

Of the 5151 randomly selected GPs invited to participate in the panel, 695 could not be contacted, and 732 were not eligible; 1712/3724 eligible GPs (46.0%) agreed to participate. GPs who refused were more often men ($P < 10^{-3}$), older ($P < 10^{-3}$), and had more

consultations in 2012 ($P < 0.05$, Table 1). They reported two main reasons for refusing: lack of time (55%) and lack of interest in participating in a panel (31%). In all, 1582/1712 GPs (92.4%) participated in the cross-sectional survey: their characteristics did not differ significantly from those of the GPs who joined the panel but did not participate in the vaccination survey (Table 1).

The frequency of GPs' vaccine recommendations to their patients varied according to the vaccine situation (Table 2): 83% of the participants reported that they would often or always recommend vaccination against measles, mumps and rubella (MMR) for non-immune adolescents and young adults, 68% would recommend vaccination against meningococcal meningitis C for infants aged 12 months, but only 57% for the group aged 2–24 years (Table 2). Over 80% of the participants trusted official sources (Ministry of Health, health agencies, scientists, or specialist colleagues) to provide reliable information about vaccine benefits and risks (Table 2). GPs' opinions of the likelihood of severe adverse effects of vaccines also varied according to vaccine: 6% of the participants considered a link between HPV vaccines and multiple sclerosis likely or very likely, while 33% responded positively to the question about a link between adjuvanted vaccines and long-term complications. More than a quarter (26%) agreed somewhat or strongly that some vaccines recommended by the authorities are not useful and 20% that children are vaccinated against too many diseases. Only 43% of the participants felt confident explaining the role of adjuvants to their patients (Table 2).

Overall, 89% of the participants reported that at least one of their patients had had at least one of the vaccine-preventable diseases mentioned in the questionnaire in the past 5 years.

Multivariable logistic regressions of the dichotomized global score of vaccine recommendations (Table 3) showed that GPs' vaccine recommendations to patients were more frequent when they were comfortable explaining benefits and risks to patients, or trusted official sources of information highly than when they did not. Their recommendations were less frequent when they believed serious adverse effects to be likely, or doubted the vaccine's utility than when they did not.

Looking at the dichotomized subscore for recommendations of uncontroversial vaccines, we found results similar to those for the global score, above, for comfort in ability to explain benefits and risks and for doubts about vaccine utility. On the other hand, trusting official sources about vaccination and opinions about potential severe adverse effects were not associated with this subscore.

We found no issue of multicollinearity in the linear models and, as multicollinearity is a property of the explanatory variables, not the dependent variable (Allison, 2012), we can conclude that there was no issue of multicollinearity in the logistic models either. The results of the LR tests for the bivariate probit model with sample selection showed no significant correlation for either recommendation score (global score: rho = 0.05, $P = 0.97$; score for uncontroversial vaccines: rho = 0.18; $P = 0.89$). Dichotomization of the scores with a threshold at mean + 1 standard deviation rather than the median produced similar estimates of the odds ratios for the variables of interest. The multivariable logistic regression of the dichotomized global score of vaccine recommendations, adjusted for the four stratification variables, showed that GPs' recommendations to patients were significantly associated with their own vaccination behavior (2013–2014 seasonal influenza: ORa = 2.95, 95% CI = [2.31;3.77]; 3 doses or more of hepatitis B vaccine: 1.90 [1.27;2.84]).

4. Discussion

Our study addresses the attitudes and behaviors of a large national sample of GPs regarding several vaccines and target populations. Although their self-reported vaccine recommendations to their patients varied substantially according to the situation, these recommendations were nonetheless somewhat consistent. They were more consistent and frequent when GPs were comfortable in their ability to explain the benefits and risks of vaccines and when they trusted official sources of information highly; they were less consistent and less frequent for GPs who expressed doubts about the harmlessness and, above all, the utility of some recommended vaccines. On the contrary, however, for the vaccines against meningitis C and MMR, that is, vaccines which are not controversial in France (see Appendix, Table A1), the frequency of GPs' recommendations was no longer associated with either trusting official sources of information or expressing doubts about harmlessness.

Given that by joining the panel, GPs agreed to take part in five different surveys during a 30-month period, the commitment rate (46%) was high, higher than in other primary physician panels (Joyce et al., 2010). To limit potential selection bias that could have resulted from particular opinions or attitudes about vaccination, this topic was not mentioned to GPs before they were asked to consent to participate in the panel. Panel participants differed from non-participants for several characteristics (sex, age and workload), and these characteristics were associated with the vaccine recommendation scores (Table 3). But weighting the sample according to sex, age and workload should have corrected this selection bias and prevented any impact on the recommendation scores. Moreover, the lack of significance of the LR tests for the bivariate probit models with sample selection gives us confidence that the estimates of the logistic regression models were not biased.

Vaccine recommendation behaviors were self-reported, which is a limitation of our study: declaration or desirability biases cannot be excluded. However, questionnaire data appears to overestimate vaccination rates by less than 10% (Brien et al., 2012), and self-reported pandemic or seasonal influenza vaccination coverage in hospital healthcare workers has been shown to be a good proxy for recorded vaccine coverage (Llupià et al., 2012). Validating the self-reported data by retrieving reliable information about GPs'behaviors from patients' files was not feasible, even for a limited sample of GPs, especially as very few GPs in private practices consistently record data about patients and consultations. The Cronbach alpha of the scores for vaccine recommendations (0.74 and 0.63) and principal component analyses confirmed the internal validity of the scores.

Moreover, several reasons indicate that these scores are better proxies for VH than the separate study of each vaccine situation separately. First, the notion of VH is defined by a variety of behaviors and attitudes toward different vaccine situations, not by a single, unidimensional approach of opposition (Larson et al., 2014; Dubé et al., 2013). Second, GPs' self-reported recommendation frequency may also reflect in part the degree to which they are favorable to vaccines (Larson et al., 2014; Peretti-Watel et al., 2015). Finally, the strong association between the recommendation scores and GPs' own vaccination behavior scores confirms the robustness of the global score as a proxy for VH.

Two final weaknesses must be noted. Because this vaccination survey is cross-sectional and retrospective, no causal inferences can be drawn. In addition, because VH depends highly on context, it is possible that our results cannot be extrapolated to other countries, where no or different vaccine controversies have occurred (Larson et al., 2014).

There are few published studies of GPs' vaccine recommendation behavior for most of the situations examined in our study. In France, François et al. found that 14% of GPs never or sometimes recommend hepatitis B vaccines to adolescents (37% in our study) (François et al., 2011). In Minnesota, McRee et al. found that 24% of health care providers most often do not recommend HPV vaccines to young girls (28% in our study) (McRee et al., 2014). Our findings show that GPs' vaccine recommendations vary according to the vaccine situation and thus suggest that VH is prevalent among French GPs. The recommendation scores allowed us to capture this hesitancy. GPs' VH may contribute to the suboptimal vaccine coverage for the vaccines and target groups considered in this study. The absence of physicians' recommendations has been reported as an important reason for non-vaccination against various vaccine-preventable diseases (Schwarzinger et al., 2010; Holman et al., 2014; Zimmerman et al., 2003). Hesitant physicians are less likely to try to convince hesitant or reluctant patients to be

vaccinated. They may also be less likely to address — satisfactorily or at all — patients' questions about vaccination safety and risks of contracting illnesses, the two reasons patients give most frequently for their own VH (Yaqub et al., 2014).

Our findings shed light on reasons for VH among GPs. Consistent with our first hypothesis, doubts about the utility of certain vaccines, and lack of self-efficacy, both of which probably reflect GPs' enduring beliefs and attitudes, were associated with the global vaccine recommendation score and the subscore. Distrust of health authorities and experts and a perception of severe adverse effects of vaccines — both variables related to the existence of past and ongoing controversies — were not associated with uncontroversial vaccines but only with the global score. This finding confirms our second hypothesis.

Previous results in France and elsewhere have reported prevalence rates of doubts about vaccine utility ranging between 22% and 37% among physicians (Dubé et al., 2013; François et al., 2011; Bruno et al., 2014). Our findings suggest that such doubts are a stronger factor in GPs' VH than is their perception of side effects. These doubts may also be linked to a tendency of some GPs to criticize official recommendations and guidelines, for example, because they consider them too constraining and ill adapted to the reality of practice and patients (Clerc et al., 2011). GPs often identify the complexity of the vaccine schedule and its annual modifications for new vaccines and new guidelines as constraints (Larson et al., 2011; François et al., 2011).

The directions of the links observed between GPs' self-efficacy level in explaining the benefits and risks of vaccines or the role of adjuvants and their global vaccine recommendation score (as well as the subscore for uncontroversial vaccines) could not be disentangled in this cross-sectional study. GPs' lack of self-efficacy may contribute to their VH, which in turn could also reduce their self-efficacy. This self-efficacy may be affected by the paucity of initial training in the field of vaccination (Yaqub et al., 2014; Cabana et al., 1999; Pulcini et al., 2014), which does not prepare them for the new challenges of communication with patients in contemporary societies (Edwards et al., 2002).

Few studies have addressed GPs' trust toward various stakeholders when studying their vaccination behaviors (Bish et al., 2011). Only a minority of GPs strongly trusted health authorities and public health agencies, and distrust toward them was not infrequent. These findings were contrary to those about GPs' attitudes regarding scientific sources (Table 2). Our results suggest that low or moderate trust in health authorities and experts (Table 3) may contribute, independently of other factors, to VH among GPs for controversial vaccines. Past and ongoing controversies in France may have played — and may still play — a part in this distrust: the decision to suspend the school-based hepatitis B vaccination program in 1998 (Larson and Heymann, 2010) and the 2009 pandemic vaccination campaign might have durably affected GPs' trust in health authorities. The latter, in particular, excluded GPs from its preparation and implementation (Schwarzinger et al., 2010), a factor that negatively influenced their recommendations of the pandemic vaccine to patients (Verger et al., 2012; Flicoteaux et al., 2014). Although discussing the causes of GPs' reduced or lack of trust toward health authorities and experts is beyond the scope of this article, our results should prompt an in-depth reflection of how health authorities communicate with private GPs and involve them in public health issues such as vaccination.

Others have reported that physicians may have fears or doubts about serious adverse effects of vaccines (François et al., 2011; Poland, 2010; Verger et al., 2012; Daley et al., 2010), as we observed here. Our findings suggest that these perceptions — probably reflecting sensitivity to vaccine controversies, as most of those in France have focused on vaccines' side effects — contribute to VH among GPs, but only for controversial vaccines (Table 3). Examining the pattern of these perceptions according to each situation separately (Table 2) suggests that they reflect a dimension that is more attitudinal than evidence-based because we found that the GPs' answers were not thoroughly consistent with the scientific evidence about vaccine adverse effects. GPs' negative perceptions of aluminum as an adjuvant are not surprising in the French context: this particular adjuvant has been the object of debate in France since 1998 when a group of French scientists published the first of several articles arguing that aluminum in vaccines can cause macrophagic myofasciitis (localized lesions at the vaccination site, containing aluminum salts) and long-term systemic adverse effects (Gherardi et al., 1998; Gherardi et al., 2001; Couette et al., 2009). Both the WHO Global Advisory Committee on Vaccine Safety and the French Public Health Council, the latter in a detailed scientific report in 2013 (Haut Conseil de la Santé Publique, 2013), agree that localized lesions occur in a small number of vaccine patients, but find no evidence to suggest that they are associated with a resulting clinical illness or disease (Table A1, Appendix). This controversy, essentially limited to France, has been simmering for more than a decade, fuelled by one group of researchers and one association of patients and prolonged by the difficulty of proving negatives and might well have contributed to the spread of doubts among French doctors. Public health authorities and medical educators must find effective strategies for addressing these attitudes among GPs.

Convincing vaccine-hesitant patients to be vaccinated requires a response to GPs' VH. Necessary steps include both better training and updating of GPs' knowledge of vaccines' benefits and risks: more time must be devoted to vaccination during medical studies than is currently spent. Training should also aim at improving GPs' skills for communicating with vaccine-hesitant or reluctant patients. Initiatives such as the guide “Let's talk about protection” can build the foundations for developing such approaches, but they have not been offered to doctors in the field of vaccination in France, as they have been elsewhere (European Centre for Disease Prevention and Control, 2012). However, these training tools and methods should also be evaluated for effectiveness. Finally, GPs and other doctors need supporting tools that provide them with arguments to respond to allegations on the Internet or in the news media: these tools should be regularly updated to new perceptions and rumors. This would require the permanent monitoring of various media, an approach that already exists in various fields due to the progress of data mining technologies (Larson et al., 2013).

5. Research in Context

Our study of 1582 French GPs shows that they sometimes hesitate to recommend vaccines against measles, hepatitis B, meningitis C, human papilloma virus, or seasonal flu to their patients for whom the health authorities recommend them. This hesitancy is especially marked for GPs who do not have confidence in health authorities, who express doubts about their harmlessness, do not feel comfortable explaining the benefits and risks of vaccines to patients, or are not convinced of the general utility of vaccines. Given GPs' essential role in vaccination, this may contribute to insufficient coverage for these vaccines.

6. Conclusion

Overall our findings suggest that VH is prevalent among French GPs. It may make them ill at ease in addressing their patients' concerns about vaccination, which in turn might reinforce patients' VH (Gowda and Dempsey, 2013).

More research is warranted to assess VH among GPs and other health care workers for an extended set of vaccines, target populations, and countries. Better understanding of the determinants of VH among physicians is also necessary, in particular to assess the extent to which patients' VH contributes to physicians' VH (Peretti-Watel et al., 2015; McRee et al., 2014). Our findings also call for the development and evaluation of interventions and tools targeting GPs to contain and restrain their VH and help them cope with patients' VH. GPs would benefit from tools and training focusing on communication skills to address their patients' concerns about vaccination (European Centre for Disease Prevention and Control, 2012). Another important aspect lies in

addressing their distrust of the health authorities: this is not a simple task, as it necessitates changes far beyond the vaccination field.

Contributors

FC, AG, CJ, HL, OL, JR, CP and PPW designed the questionnaire and critically revised the manuscript.

PV conceived, designed and supervised the study, interpreted its data, and drafted the manuscript.

LF performed the statistical analysis, interpreted the data, and critically revised the manuscript.

Declaration of Interests

None of the authors has any conflict of interest to declare except CP who reports non-financial support from Pfizer, non-financial support from Sanofi Pasteur, unrelated to the work reported here.

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Appendix A. Supplementary data

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References

Allison, P.D., 2012. Logistic Regression Using SAS: Theory and Application. Second Edition. SAS Institute.
Bandura, A., 1994. Self-efficacy. In: Ramachaudran, V.S. (Ed.), Encyclopedia of Human Behavior. New York, pp. 71–81.
Bean, S.J., Catania, J.A., 2013. Vaccine perceptions among Oregon health care providers. Qual. Health Res. 23, 1251–1266. http://dx.doi.org/10.1177/1049732313501891.
Benin, A.L., Wisler-Scher, D.J., Colson, E., Shapiro, E.D., Holmboe, E.S., 2006. Qualitative analysis of mothers' decision-making about vaccines for infants: the importance of trust. Pediatrics 117, 1532–1541. http://dx.doi.org/10.1542/peds.2005-1728.
Bish, A., Yardley, L., Nicoll, A., Michie, S., 2011. Factors associated with uptake of vaccination against pandemic influenza: a systematic review. Vaccine 29, 6472–6484. http://dx.doi.org/10.1016/j.vaccine.2011.06.107.
Bland, J.M., Altman, D.G., 1997. Statistics notes: Cronbach's alpha. Br. Med. J. 314, 572.
Brien, S., Kwong, J.C., Buckeridge, D.L., 2012. The determinants of 2009 pandemic A/H1N1 influenza vaccination: a systematic review. Vaccine 30, 1255–1264. http://dx.doi.org/10.1016/j.vaccine.2011.12.089.
Bruno, D.M., Wilson, T.E., Gany, F., Aragones, A., 2014. Identifying human papillomavirus vaccination practices among primary care providers of minority, low-income and immigrant patient populations. Vaccine 32, 4149–4154. http://dx.doi.org/10.1016/j.vaccine.2014.05.058.
Cabana, M.D., Rand, C.S., Powe, N.R., Wu, A.W., Wilson, M.H., 1999. Why don't physicians follow a framework for improvement. JAMA 282, 1458–1465.
Clerc, I., Ventelou, B., Guerville, M.-A., Paraponaris, A., Verger, P., 2011. General practitioners and clinical practice guidelines: a reexamination. Med. Care Res. Rev. 68, 504–518. http://dx.doi.org/10.1177/1077558710397761.
Couette, M., Boisse, M.-F., Maison, P., et al., 2009. Long-term persistence of vaccine-derived aluminum hydroxide is associated with chronic cognitive dysfunction. J. Inorg. Biochem. 103, 1571–1578. http://dx.doi.org/10.1016/j.jinorgbio.2009.08.005.
Daley, M.F., Crane, L.A., Markowitz, L.E., et al., 2010. Human papillomavirus vaccination practices: a survey of US physicians 18 months after licensure. Pediatrics 126, 425–433. http://dx.doi.org/10.1542/peds.2009-3500.
Dubé, E., Laberge, C., Guay, M., Bramadat, P., Roy, R., Bettinger, J., 2013. Vaccine hesitancy: an overview. Hum. Vaccin. Immunother. 9, 1763–1773. http://dx.doi.org/10.4161/hv.24657.
Ecole des Hautes Etudes en Santé Publique., 2013. Faciliter l'accès aux vaccinations en s'appuyant sur les Agences Régionales de Santé.
Edwards, N., Kornacki, M.J., Silversin, J., 2002. Unhappy doctors: what are the causes and what can be done? BMJ 324, 835–838. http://dx.doi.org/10.1136/bmj.324.7341.835.
European Centre for Disease Prevention and Control., 2012. Let's Talk About Protection. ECDC, Stockholm (http://ecdc.europa.eu/en/healthtopics/immunisation/comms-aid/Documents/Vaccine-comms-action-2013.pdf).
European Centre for Disease Prevention and Control, 2012. Communication on Immunisation — Building Trust. ECDC, Stockholm (http://ecdc.europa.eu/en/publications/Publications/TER-Immunisation-and-trust.pdf).
Flicoteaux, R., Pulcini, C., Carrieri, P., Schwarzinger, M., 2014. Correlates of general practitioners' recommendations to patients regarding vaccination for the 2009–2010 pandemic influenza (A/H1N1) in France: implications for future vaccination campaigns. Vaccine 32, 2281–2287. http://dx.doi.org/10.1016/j.vaccine.2014.02.074.
François, M., Alla, F., Rabaud, C., Raphaël, F., 2011. Hepatitis B virus vaccination by French family physicians. Médecine Mal. Infect. 41, 518–525. http://dx.doi.org/10.1016/j.medmal.2011.07.002.
Freed, G.L., Clark, S.J., Cowan, A.E., Coleman, M.S., 2011. Primary care physician perspectives on providing adult vaccines. Vaccine 29, 1850–1854. http://dx.doi.org/10.1016/j.vaccine.2010.12.097.
Gherardi, R.K., Coquet, M., Chérin, P., et al., 1998. Macrophagic myofasciitis: an emerging entity. Lancet 352, 347–352. http://dx.doi.org/10.1016/S0140-6736(98)02326-5.
Gherardi, R.K., Coquet, M., Cherin, P., et al., 2001. Macrophagic myofasciitis lesions assess long-term persistence of vaccine-derived aluminium hydroxide in muscle. Brain 124, 1821–1831. http://dx.doi.org/10.1093/brain/124.9.1821.
Gowda, C., Dempsey, A.F., 2013. The rise (and fall?) of parental vaccine hesitancy. Hum. Vaccin Immunother. 9, 1755–1762. http://dx.doi.org/10.4161/hv.25085.
Greene, W.H., 2003. Econometric Analysis. 5th ed. Prentice Hall, Upper Saddle River, NJ.
Gust, D.A., Darling, N., Kennedy, A., Schwartz, B., 2008. Parents with doubts about vaccines: which vaccines and reasons why. Pediatrics 122, 718–725. http://dx.doi.org/10.1542/peds.2007-0538.
Haut Conseil de la Santé Publique, 2013. Aluminium et vaccins. http://www.hcsp.fr/explore.cgi/avisrapportsdomaine?clefr=369.
Heckman, J.J., 1979. Sample selection bias as a specification error. Econometrica 47, 153–161.
Holman, D.M., Benard, V., Roland, K.B., Watson, M., Liddon, N., Stokley, S., 2014. Barriers to human papillomavirus vaccination among US adolescents: a systematic review of the literature. JAMA Pediatr. 168, 76–82. http://dx.doi.org/10.1001/jamapediatrics.2013.2752.
Joyce, C.M., Scott, A., Jeon, S.-H., et al., 2010. The 'medicine in Australia: balancing employment and life (MABEL)' longitudinal survey—protocol and baseline data for a prospective cohort study of Australian doctors' workforce participation. BMC Health Serv. Res. 10, 50. http://dx.doi.org/10.1186/1472-6963-10-50.
Larson, H.J., Heymann, D.L., 2010. Public health response to influenza A(H1N1) as an opportunity to build public trust. JAMA 303, 271–272. http://dx.doi.org/10.1001/jama.2009.2023.
Larson, H.J., Cooper, L.Z., Eskola, J., Katz, S.L., Ratzan, S., 2011. Addressing the vaccine confidence gap. Lancet 378, 526–535. http://dx.doi.org/10.1016/S0140-6736(11)60678-8.
Larson, H.J., Jarrett, C., Eckersberger, E., Smith, D.M.D., Paterson, P., 2014. Understanding vaccine hesitancy around vaccines and vaccination from a global perspective: a systematic review of published literature, 2007–2012. Vaccine 32, 2150–2159. http://dx.doi.org/10.1016/j.vaccine.2014.01.081.
Larson, H.J., Smith, D.M.D., Paterson, P., et al., 2013. Measuring vaccine confidence: analysis of data obtained by a media surveillance system used to analyse public concerns about vaccines. Lancet Infect. Dis. 13, 606–613. http://dx.doi.org/10.1016/S1473-3099(13)70108-7.
Llupià, A., García-Basteiro, A.L., Mena, G., et al., 2012. Vaccination behaviour influences self-report of influenza vaccination status: a cross-sectional study among health care workers. PLoS ONE 7, 1–5. http://dx.doi.org/10.1371/journal.pone.0039496.
McRee, A.-L., Gilkey, M.B., Dempsey, A.F., 2014. HPV vaccine hesitancy: findings from a statewide survey of health care providers. J. Pediatr. Health. Care 28, 1–9. http://dx.doi.org/10.1016/j.pedhc.2014.05.003.
Obrizan, M., 2010. Essays on Selection in Health Survey Data.
Peretti-Watel, P., Larson, H., Ward, J., Schulz, W., Verger, P., 2015. Vaccine hesitancy: clarifying a theoretical framework for an ambiguous notion. PLoS Curr. Outbreaks http://dx.doi.org/10.1371/currents.outbreaks.6844c80ff9f5b273f34c91f71b7fc289.
Poland, G.A., 2010. The 2009–2010 influenza pandemic: effects on pandemic and seasonal vaccine uptake and lessons learned for seasonal vaccination campaigns. Vaccine 28 (Suppl. 4), D3–D13. http://dx.doi.org/10.1016/j.vaccine.2010.08.024.
Pulcini, C., Massin, S., Launay, O., Verger, P., 2013. Factors associated with vaccination for hepatitis B, pertussis, seasonal and pandemic influenza among French general practitioners: a 2010 survey. Vaccine 31, 3943–3949. http://dx.doi.org/10.1016/j.vaccine.2013.06.039.
Pulcini, C., Massin, S., Launay, O., Verger, P., 2014. Knowledge, attitudes, beliefs and practices of general practitioners towards measles and MMR vaccination in southeastern France in 2012. Clin. Microbiol. Infect. 20, 38–43. http://dx.doi.org/10.1111/1469-0691.12194.
Rogerson, P., 2001. Statistical Methods for Geography. SAGE.
SAGE Group, 2014. http://www.who.int/immunization/sage/sage_wg_vaccine_hesitancy_apr12/en/.
Schwarzinger, M., Verger, P., Guerville, M.-A., et al., 2010. Positive attitudes of French general practitioners towards A/H1N1 influenza-pandemic vaccination: a missed opportunity to increase vaccination uptakes in the general public? Vaccine 28, 2743–2748. http://dx.doi.org/10.1016/j.vaccine.2010.01.027.
Tavakol, M., Dennick, R., 2011. Making sense of Cronbach's alpha. Int. J. Med .Educ. 2, 53–55. http://dx.doi.org/10.5116/ijme.4dfb.8dfd.
Verger, P., Flicoteaux, R.R., Schwarzinger, M., et al., 2012. Pandemic influenza (A/H1N1) vaccine uptake among French private general practitioners: a cross sectional study in 2010. PLoS ONE 7, e41837. http://dx.doi.org/10.1371/journal.pone.0041837.
Yaqub, O., Castle-Clarke, S., Sevdalis, N., Chataway, J., 2014. Attitudes to vaccination: a critical review. Soc. Sci. Med. 112C, 1–11. http://dx.doi.org/10.1016/j.socscimed.2014.04.018.
Zimmerman, R.K., Santibanez, T.A., Fine, M.J., et al., 2003. Barriers and facilitators of pneumococcal vaccination among the elderly. Vaccine 21, 1510–1517. http://dx.doi.org/10.1016/S0264-410X(02)00698-9.