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## Title page

# Effect of Internet use for searching information on vaccination on the uptake of human papillomavirus vaccine in France: a path-analysis approach

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## Abstract

Internet is a popular source of information regarding vaccination. This study aimed to determine whether there is a negative association between Internet use among French vaccine-hesitant mothers and HPV vaccine uptake by their daughters, and to gain insight into the pathways that would link Internet use to the lack of HPV vaccine uptake. We conducted a pooled cross-sectional analysis across the 2015, 2016, 2017 and 2018 Vaccinoscopie® Survey. Multivariate logistic regression and path models were used in the analysis. The study sample included a total of 2038 respondent mothers. Of those, 89 (4.4%) declared having never been in the situation of searching for information regarding a vaccination they had hesitated about, leaving 1949 mothers for the present analysis. Approximately 24% (466/1949) of the mothers declared using the Internet as a source of vaccine information. In multivariate logistic regression adjusted for physician recommendation of HPV vaccination, attitudes towards vaccines in general, perception of HPV vaccine usefulness, maternal level of education, region of residence, and the survey year, the use of Internet by the mothers was significantly associated with a lower HPV vaccination among their daughters (adjusted odds ratio (aOR), 0.66; 95% confidence interval (CI), 0.47-0.91). Path analysis further confirmed the negative effect of Internet use ( $\beta = -0.10$ , standard error (SE)=0.02,  $P < 0.0001$ ), highlighting how the Internet plays a detrimental role in HPV vaccine uptake through a lower perceived level of HPV vaccine usefulness, a lower perceived level of information on childhood vaccination, and unfavorable attitudes towards vaccination in general.

# 1 Manuscript

## 2 INTRODUCTION

3 Since its introduction in the French immunization program in 2007, the initiation rate of HPV  
4 vaccination in girls aged 15 years only reached 29.4% at its highest point, in 2018 (1). The same  
5 year, the coverage rate for a two-dose regimen among 16-year-olds girls was estimated at  
6 23.7% (2). This figure represents less than half of the target set for a two-dose regimen (3). The  
7 HPV vaccine appears among those viewed less favorably in 2016 in France (4), against the  
8 general background of a noticeable rise in vaccine hesitancy (5), which may be viewed as pretty  
9 astonishing in Pasteur's country.

10 Internet has become a popular source of information regarding health-related topics, and HPV  
11 vaccine makes no exception. Indeed, this vaccination is a popular topic among "googling"  
12 searches for vaccine-preventable infectious diseases (6). The Eurobarometer Survey on the  
13 European citizens' digital health literacy conducted in 2014 showed that around one out of two  
14 respondents in France have used the Internet to search for health-related information within  
15 the last year, 40% of whom indicated looking on behalf of their children. The French National  
16 Health Barometer Survey conducted the same year showed that as many as 69 % of the French  
17 population used the Internet to search for health-related topics (7).

18 Whilst the Internet represents a remarkable tool for health information dissemination, it also  
19 provides a medium where misinformation (misinformed advice) and disinformation (deliberate  
20 falsehoods) (8) are easily introduced, accessed and spread. This has become more problematic  
21 as we live in an era of "post-truth" (defined by Oxford dictionary as "circumstances in which  
22 objective facts are less influential in shaping public opinion than appeals to emotion and  
23 personal belief"(9)). in The use of social media (such as Facebook) and messaging platforms  
24 (such as WhatsApp) allows instant global dissemination of false information (10). This comes  
25 with its own share of challenges in the health information field. For example, one study  
26 analyzing the reach of online disinformation in Europe(9)e showed that the most popular false

27 news website in France, a website claiming to "vulgarize information on health and wellness",  
28 had received approximately as many interactions on social media (shares, comments, reactions)  
29 as five prominent and reliable French news websites combined (11). The spread of  
30 misinformation on the benefits and risks of vaccines has certainly been fueling vaccine hesitancy  
31 (12)(13)(14)(15), although it remains to be seen to what extent this translates into the decision  
32 to vaccinate. The World Health Organization has listed the "uncontrolled dissemination of  
33 misinformation" - including in the field of vaccination - among its urgent health challenges for  
34 the next decade (16).

35 HPV vaccination in France provides an interesting case study of challenges facing vaccination in  
36 an era of online mis/disinformation, as the introduction of the HPV vaccine in the French  
37 vaccine immunization program has coincided more or less with the rise of social media  
38 utilization. Furthermore, HPV vaccination in France is delivered opportunistically through  
39 healthcare providers, with no dedicated school-based vaccination program. Therefore, parents  
40 who have not heard about the HPV vaccine from their healthcare providers may have questions  
41 to be answered about this vaccination.

42 In this context, we aimed to determine whether there was a negative association between  
43 Internet use among French vaccine-hesitant mothers and HPV vaccine uptake by their  
44 daughters, and to gain insight into the pathways that would link Internet use to a lack of HPV  
45 vaccine uptake. Such an understanding is required to fully appreciate the impact of the Internet  
46 on the uptake of HPV vaccination in France, and provide relevant data for policymakers and  
47 practitioners to take necessary action.

## 48 **METHODS**

### 49 **Data source**

50 This study was carried out using the data acquired from the 2015, 2016, 2017 and 2018  
51 Vaccinoscopie® Survey modules targeting mothers of girls aged 14 and 15 years. The  
52 methodology of this survey commissioned by GlaxoSmithKline (GSK) and conducted by IDM  
53 Families, an independent market research and polling company, has been published in detail

54 elsewhere (17)(18). Briefly, Vaccinoscopie® is a pluriannual web-based survey among French  
55 representative quota samples of mothers, with respect to the socio-professional category (SPC)  
56 of the reference person in the household, the number of children, and the geographic region of  
57 residence, per child's years of age. It has been designed to monitor the dynamics of childhood  
58 vaccine coverage, and perception and attitudes towards vaccination in France. A new sample of  
59 study participants is interrogated from one year to another.

## 60 **Study variables**

61 The dependent variable was HPV vaccine initiation (i.e., the receipt of at least one dose of HPV  
62 vaccine) in the 14-15 year-old daughter. The exposure of interest was "Internet use by the  
63 mother" (yes/no), given the mother's answers to the question "When you hesitate about a  
64 vaccine, what source(s) of information do you turn to to decide whether or not to have your  
65 child vaccinated?". This question had a multiple-choice response format. For the purpose of this  
66 analysis, we derived a dummy variable for each source of information.

67 Guided by reviews of the literature on the factors associated with HPV vaccine uptake (19)  
68 (20)(21), we took into account the following relevant factors in the association between the  
69 exposure of interest and the dependent variable: 1) mother's demographics and socioeconomic  
70 stratus: age, level of education, household income and geographical region of residence; 2)  
71 maternal attitudes towards vaccination in general (response to the single answer question "How  
72 do you feel about vaccines?": in favour of vaccinating against all serious diseases if there are  
73 vaccines/ in favour of minimizing the number of vaccinations/ opposed to all vaccines/ no  
74 opinion), and perception of HPV vaccine usefulness (response to the single answer question  
75 "For each of these diseases (cervical cancer), supposing there was a vaccine, would vaccinating  
76 your child seem: indispensable/ useful/ not very useful/ useless/ do not know"); 3) physician  
77 recommendation of HPV vaccination (response to the single answer question "Has your doctor  
78 advised you to have your child vaccinated against HPV": yes/ no/ do not remember); 4)  
79 perceived level of information regarding childhood vaccination (response to the single answer  
80 question: "Do you think you are well informed about child vaccinations?": not at all well-  
81 informed/ rather not well-informed/ rather well-informed/ fully informed and); and 5)

82 daughter's usual medical follow-up setting (response to the single answer question : "Your child  
83 is followed by : a general practice/ a pediatrician practice/ a free preventive clinic for mother  
84 and infants").

## 85 **Statistical analysis**

86 We conducted a pooled cross-sectional analysis across the four aforementioned years of the  
87 Vaccinoscopie® Survey. We combined these data sets in order to achieve a large enough sample  
88 size to perform multivariate analysis. The data sets included data weighted according to the  
89 French general population census of the French National Institute for Statistics and Economic  
90 Studies. Although the data were generated each year from a quota sample and not from a  
91 random probability one, we decided to conduct inferential statistical analysis commonly used to  
92 make inferences about the larger population from which the sample was drawn. Since it is  
93 difficult to guarantee that the study sample is representative for characteristics other than  
94 those for which quotas units have been set, inferential statistical measures (95% confidence  
95 intervals (95%CI) and P-values) are meant only for indicative purposes in the present study.

### 96 ***Logistic regression analysis***

97 We conducted a descriptive analysis of study variables followed by a bivariate analysis, where  
98 HPV vaccine initiation was regressed on the covariates, which were were assessed for  
99 multicollinearity beforehand. We then estimated a multivariate logistic regression model using a  
100 backward selection process, with a threshold of  $P=0.20$  for a variable to stay in the model. The  
101 full model included the year of the Vaccinoscopie® Survey, in addition to the aforementioned  
102 exposure variable and covariates. For ease of interpretation, we used the grouping of response  
103 modalities required by the path analysis described below. The goodness-of-fit of the final model  
104 was tested using the information matrix test.

105 Crude and adjusted odds ratios were calculated with their 95%CI.

### 106 ***Path analysis***

107 We formulated a general hypothetical model for how Internet use, attitudes towards childhood  
108 vaccination, perceived usefulness of HPV vaccine, and the other above mentioned factors might  
109 be interrelated to HPV vaccine uptake. The hypothesized interrelationships between the

110 variables are depicted in a conceptual model in **Figure 1**. To test our proposed hypothetical  
111 model, we applied path analysis, a form of statistical modeling consisting of a set of linear  
112 equations that simultaneously assess the relationships between the measured variables. We  
113 conducted these analyses using the PROC CALIS procedure in SAS with the weighted least  
114 squares (WLS) estimation method, which handles categorical variables (22). Nominal variables  
115 with more than two categories of response modalities (geographic area of residence, perceived  
116 usefulness of HPV vaccine, attitudes towards childhood vaccination, and perceived level of  
117 information) were dichotomized by grouping responses modalities, as the PROC CALIS  
118 procedure handles continuous, binary and ordinal variables, but not nominal variables.

119 We first tested the hypothesized conceptual model, which included all possible associations  
120 between variables (**Figure 1**). Afterward, we reviewed the path coefficients to see if any of the  
121 paths in the initial model should be deleted, and we dropped non-significant associations from  
122 the original hypothetical model. The resulting model, called the “final model”, was then re-  
123 estimated (**Figure 2**). We used standardized regression coefficients ( $\beta$ ) to assess the strength of  
124 association between the variables (effect). Total, direct, and indirect effects of each variable on  
125 HPV vaccine uptake were estimated (a direct effect represents a path coefficient, an indirect  
126 effect represents the product of sequential path coefficients, and a total effect represents the  
127 sum of direct and indirect effects).

128 We used Cohen's recommendations to interpret the relative size effect of the standardized  
129 coefficients (a  $\beta$  value varying around 0.1 is considered as low, a value varying around 0.3 as  
130 moderate, and a value greater than 0.5 as large) (23). To evaluate the goodness-of-fit between  
131 the final model and the data, we used the comparative fit index (CFI), the standardized root  
132 mean square residual (SRMR), and the root-mean-square error of approximation (RMSEA)  
133 including 90%-confidence interval (90%CI). Values for CFI >0.94 suggest a good fit between data  
134 and path models, whereas SRMR and RMSEA values less than 0.090 suggest acceptable fit, and  
135 values less than 0.055 suggest good model fit (24).

136 All statistical analyses were performed using SAS (version 9.4, SAS Institute Inc., Cary North  
137 Carolina), and p-values below 0.05 were considered statistically significant.



138 **Ethics statement**

139 The Vaccinoscopie® Survey is a healthcare market research undertaken by professional market  
140 researchers (IDM families) on behalf of a pharmaceutical company (GSK). It has been conducted  
141 in accordance with the legal and ethical guidelines issued jointly by the European Society for  
142 Opinion and Market Research (ESOMAR) and the International Chamber of Commerce (ICC), as  
143 well as the French law on computer data and freedom. It does not require ethical committee  
144 review. It warrants the total confidentiality of collected data, which, in any case, cannot be  
145 used to any other end than the ones defined for the survey. Furthermore, each participant may  
146 stop answering the questionnaire at any time and refuse that some pieces of data to be  
147 processed. Study participants consented to IDM terms of use and privacy policy, which indicated  
148 that their data would be used anonymously. The Vaccinoscopy® data file was approved by the  
149 French National Committee for Data Protection (n°1551077, dated 08/12/2011).

150 **RESULTS**

151 **Study sample**

152 The global Vaccinoscopie® Survey data set (2015 to 2018) included in total 2038 different  
153 respondent mothers. Of those, 89 (4.4%) declared having never been in the situation of  
154 searching for information regarding a vaccination they had hesitated about, leaving 1949  
155 records for the present study. The mean (+/- SD) age of the survey respondents was 43.5 ( $\pm$ 4.9)  
156 years. Approximately half of the participants had a level at high school diploma (baccalaureate)  
157 or two-year post high school diploma (49.6%) and had a monthly household income of over  
158 2700 Euros (48.0%). The full characteristics of the study participants, together with their  
159 responses to the survey questionnaire, can be found in **Table 1**.

160 **HPV vaccine coverage**

161 The mean uptake of the first dose of HPV vaccine over the study period was 27.7% (23.7% in  
162 2015, 23.5% in 2016, 30.3% in 2017 and 33.1% in 2018). The full 2-dose regimen was completed  
163 in 18.7% of their daughters (14.4% in 2015, 16.1% in 2016, 21.3% in 2017 and 22.6% in 2018).

164 **Internet and other sources of vaccine information**

165 Approximately 24% of the mothers declared using the Internet as a source of vaccine  
166 information. This medium was the third most frequently cited source of information reported  
167 by the mothers, after the family physician (91.8%) and the relatives/family/friends (26.1%), and  
168 before the pharmacist (14.9%) (**Table 1**).

169 **Logistic regression analysis**

170 The uptake of the first dose of HPV vaccine was lower among daughters of the mothers who  
171 indicated using the Internet as a source of vaccine information compared to daughters of those  
172 who indicated not using it: 18% compared to 31%, respectively ( $P<0.0001$ ). In multivariate  
173 analysis adjusted for physician recommendation of HPV vaccination, attitudes towards vaccines  
174 in general, perception of HPV vaccine usefulness, maternal level of education, geographical  
175 region of residence, and the year of the survey, the use of the Internet as a source of vaccine  
176 information was significantly associated with a lower HPV vaccination (aOR=0.66; 95% CI, 0.47-  
177 0.91) (**Table 2**).

178 **Path analysis**

179 The results of the path analysis modeling are depicted in **Figure 2**. The estimated « final model »  
180 shows a good overall fit: CFI=0.97, SRMR=0.03 and RMSEA=0.02, 90%CI (0.02-0.03). Overall, 26  
181 % of the variance in HPV vaccine uptake was explained by the model. **Table 3** shows the direct,  
182 indirect, and total effects of Internet use and other sources of information on HPV vaccine  
183 uptake (effects of other variables are reported in the **Supplementary Table**). The total effect of  
184 Internet use on HPV vaccine uptake was proved to be significant and negative. It is considered  
185 as low ( $\beta=-0.10$ , Standard Error (SE)=0.02,  $P<0.0001$ ), and represents in absolute value 27% of  
186 the highest total effect on HPV vaccine uptake, which is observed with the physician  
187 recommendation of HPV vaccination ( $\beta=0.37$ , SE=0.01,  $P<0.0001$ ) (**Table 3 and Supplementary**  
188 **Table**).

189 A total of 4 paths were significant to explain the relationship between Internet use and HPV  
190 vaccine uptake:

- 191 1) Internet use -> perceived level of information regarding childhood vaccination->  
192 attitudes towards vaccines in general -> perception of HPV vaccination usefulness ->  
193 HPV vaccination;
- 194 2) Internet use -> perceived level of information regarding childhood vaccination ->  
195 attitudes towards vaccines in general -> HPV vaccination;
- 196 3) Internet use -> attitudes towards vaccines in general -> perception of HPV vaccination  
197 usefulness -> HPV vaccination;
- 198 4) Internet use -> attitudes towards vaccines in general -> HPV vaccination (**Figure 2**).  
199

200 Internet use was also found to mediate the negative effect of the « family and friends » source  
201 of information on HPV vaccine uptake ( $\beta=-0.10$ ,  $SE=0.02$ ,  $P<0.0001$ ), as Internet use was  
202 positively associated with this source of information ( $\beta=0.10$ ,  $SE=0.02$ ,  $P<0.0001$ ). In reverse,  
203 Internet use was negatively associated with the «family physician» source of information ( $\beta=-$   
204  $0.28$ ,  $SE=0.03$ ,  $P<0.0001$ ), which was found to have a total positive effect on HPV vaccine uptake  
205 ( $\beta=0.08$ ,  $SE=0.01$ ,  $P<0.0001$ ).

## 206 **DISCUSSION**

207 The spread of false information online and its influence on vaccination have been frequently  
208 addressed in the literature. However, the quantification of the effect of Internet use as a  
209 resource for answering questions on vaccination on actual vaccine uptake is much less  
210 documented. We found that maternal search for vaccine information in the Internet was  
211 associated with a lower HPV vaccination initiation by their daughters. This result is congruent  
212 with the findings of the 2016 French National Health Barometer, in which parents of children  
213 aged 1 to 15 who relied uniquely on the Internet for information on vaccination were less likely  
214 to vaccinate their children against diphtheria, tetanus, and pertussis (25). Path analysis further  
215 confirmed the negative effect of Internet use on HPV vaccine uptake ( $\beta=-0.10$ ,  $SE=0.02$ ,  
216  $P<0.0001$ ). The analysis further revealed how Internet mediated its effect through a lower  
217 perceived level of information on childhood vaccination (which could be explained by the  
218 confusion resulting from contradicting pieces of information found on the Internet),

219 unfavorable attitudes towards vaccination in general, and a lower perceived level of HPV  
220 vaccine usefulness. This effect runs contrary to the positive effect of obtaining information from  
221 a family physician ( $\beta=0.08$ ,  $SE=0.01$ ,  $P<0.0001$ ), through more favorable attitudes towards  
222 vaccines and higher perception of HPV vaccine usefulness.

223 The Internet affords unprecedented opportunities for finding answers to health questions, but  
224 also poses some challenges for its users. Parents should take complete responsibility to base  
225 their vaccination decision on accurate information, wisely and consciously choosing their  
226 sources of information whenever questions arise as to the benefit, efficacy or safety of any  
227 given vaccine. Until each and every parent is equipped with the necessary knowledge and skills  
228 to interrogate the Internet safely, healthcare providers remain the most suitable and accurate  
229 sources of information on the topic of vaccination, and parents should be encouraged to seek  
230 information primarily from them. Interventions should be designed to empower parents to  
231 better recognize mis/disinformation, and consult only reputable sources of information if they  
232 wish to go online. In any case, the need to question the veracity of the information retrieved  
233 online should be emphasized, as it is sometimes not easy to distinguish between trustworthy  
234 and questionable websites.

### 235 **Strengths and limitations**

236 To the best of our knowledge, this is the first study investigating the association between  
237 Internet use as a source of information by vaccine-hesitant mothers and the uptake of HPV  
238 vaccine by their daughters. A key strength of this study is the use of path analysis to examine  
239 specific pathways by which Internet use among vaccine-hesitant mothers is associated with a  
240 lack of HPV uptake by their daughters, beyond the traditional logistic regression approach which  
241 only allows quantification of the association between two variables, all other things being  
242 equal.

243 The following limitations should be considered when interpreting the results of this study. First,  
244 the exposure measure was related to the behavior of seeking online information for vaccines in  
245 general, rather than HPV vaccine specifically. Nevertheless, only HPV vaccination is  
246 recommended in the target's age group of the daughters in the surveyed sample, hence most

247 probably the source of questioning among their mothers. Second, the quota sampling approach  
248 employed for the recruitment of the mothers in the Vaccinoscopie® Survey allows a study  
249 sample that is representative of the general population with respect to specific criteria (SPC,  
250 geographic region of residence and number of children), but does not ensure that it is  
251 representative of the general population with regard to other criteria. Therefore, caution is  
252 warranted when generalizing the results of the responding sample to the broader French  
253 population. In particular, confidence intervals and P-values have to be very carefully  
254 interpreted: they would apply if the data were obtained from a random probability sample.  
255 Furthermore, there is a possibility of selection bias through self-selection of participants, and  
256 also because the Internet population might not be fully representative of the general population  
257 (excluding the most disadvantaged groups and/or the non-French-speaking immigrants). Third,  
258 some factors possibly intervening in the process unfolding between Internet use and HPV  
259 vaccine uptake were not questioned in Vaccinoscopie® Survey and could not be introduced in  
260 our model. In a Delphi survey based on the World Health Organisation Strategy Advisory Group  
261 of Experts framework of vaccine hesitancy, we have shown that the factors possibly determining  
262 HPV vaccine uptake in France are numerous (26). These include, for example, vaccine  
263 knowledge, perception of the safety of the vaccine, and trust issues towards the health system.  
264 This may explain the direct effect observed of Internet use on HPV vaccine uptake, which  
265 probably indicates a residual effect not captured by the model variables, rather than a genuine  
266 direct effect. Fourth, this analysis was based on cross-sectional data. Therefore, causal  
267 inferences cannot be drawn, and reverse links between some variables cannot be completely  
268 ruled out. For example, the association between Internet use and perceived level of information  
269 on childhood vaccination may be due to reciprocal effects. Despite these limitations, this study  
270 seems to confirm the detrimental impact of Internet use as a source of vaccine information in  
271 vaccine-hesitant mothers. Additional studies are needed using prospective study designs among  
272 a random sample of parents.

273 **CONCLUSION**

274 In conclusion, this study found a weak but significant association between vaccine-hesitant  
275 mothers' use of the Internet as a source of vaccine information and a lack of HPV vaccine uptake  
276 by their daughters, through a lower perceived level of HPV vaccine usefulness, a lower  
277 perceived level of information on childhood vaccination, and unfavorable attitudes towards  
278 vaccination in general. While further studies are needed to confirm this link, there is no doubt  
279 on the need to raise awareness about the importance of seeking information from a healthcare  
280 provider, and consulting only reputable sources of information on the Internet.

281 **References**

- 282 1. Données de couverture vaccinale papillomavirus humains (HPV) par groupe d'âge  
283 [Internet]. [cited 2020 Aug 16]. Available from: /determinants-de-sante/vaccination/donnees-  
284 de-couverture-vaccinale-papillomavirus-humains-hpv-par-groupe-d-age
- 285 2. Fonteneau L, Barret AS, Lévy-Bruhl D. Évolution de la couverture vaccinale du vaccin  
286 contre le papillomavirus en France – 2008-2018. Bull Epidemiol Hebd. 2019;(22-23):424-30.  
287 Available from: [http://beh.santepubliquefrance.fr/beh/2019/22-23/2019\\_22-23\\_3.html](http://beh.santepubliquefrance.fr/beh/2019/22-23/2019_22-23_3.html)
- 288 3. Plan Cancer 2014-2019 - Ref : PLANKPNRT14 | Institut National Du Cancer [Internet].  
289 [cited 2018 Jan 28]. Available from: [http://www.e-cancer.fr/Expertises-et-](http://www.e-cancer.fr/Expertises-et-publications/Catalogue-des-publications/Plan-Cancer-2014-2019)  
290 [publications/Catalogue-des-publications/Plan-Cancer-2014-2019](http://www.e-cancer.fr/Expertises-et-publications/Catalogue-des-publications/Plan-Cancer-2014-2019)
- 291 4. GAUTIER A, JESTIN C, CHEMLAL K, Groupe Baromètre santé 2016. FRA. Adhésion à la  
292 vaccination en France : résultats du Baromètre santé 2016. Vaccination des jeunes enfants : des  
293 données pour mieux comprendre l'action publique. Bull Epidemiol Hebd. 2017 Oct 19;21-7.
- 294 5. Larson HJ, de Figueiredo A, Xiahong Z, Schulz WS, Verger P, Johnston IG, et al. The State  
295 of Vaccine Confidence 2016: Global Insights Through a 67-Country Survey. EBioMedicine. 2016  
296 Oct;12:295-301.
- 297 6. Bragazzi NL, Barberis I, Rosselli R, Gianfredi V, Nucci D, Moretti M, et al. How often  
298 people google for vaccination: Qualitative and quantitative insights from a systematic search of  
299 the web-based activities using Google Trends. Hum Vaccines Immunother. 2017;13(2):464-9.
- 300 7. SPF. Quelle utilisation d'Internet dans la recherche d'informations santé ? [Internet].  
301 [cited 2020 Aug 14]. Available from: /notices/quelle-utilisation-d-internet-dans-la-recherche-d-  
302 informations-sante
- 303 8. Grimes DR, Brennan LJ, O'Connor R. Establishing a taxonomy of potential hazards  
304 associated with communicating medical science in the age of disinformation. BMJ Open  
305 [Internet]. 2020 Jul [cited 2020 Aug 14];10(7):e035626. Available from:  
306 <http://bmjopen.bmj.com/lookup/doi/10.1136/bmjopen-2019-035626>
- 307 9. Dib F, Mayaud P, Chauvin P, Launay O. Online mis/disinformation and vaccine hesitancy  
308 in the era of COVID-19: Why we need an eHealth literacy revolution. Hum Vaccines Immunother  
309 [Internet]. 2021 Feb 24 [cited 2021 Mar 9];1-3. Available from:  
310 <https://www.tandfonline.com/doi/full/10.1080/21645515.2021.1874218>
- 311 10. Larson HJ. The biggest pandemic risk? Viral misinformation. Nature. 2018;562(7727):309.
- 312 11. Fletcher R, Cornia A, Graves L, Nielsen RK. Measuring the reach of “fake news” and  
313 online disinformation in Europe. :10.
- 314 12. McKee M, Middleton J. Information wars: tackling the threat from disinformation on  
315 vaccines. BMJ. 2019 May 13;365:l2144.

- 316 13. Carrieri V, Madio L, Principe F. Vaccine hesitancy and (fake) news: Quasi-experimental  
317 evidence from Italy. *Health Econ* [Internet]. 2019 Nov [cited 2020 May 21];28(11):1377–82.  
318 Available from: <https://onlinelibrary.wiley.com/doi/abs/10.1002/hec.3937>
- 319 14. Basch CH, Zybert P, Reeves R, Basch CE. What do popular YouTube™ videos say about  
320 vaccines? *Child Care Health Dev.* 2017;43(4):499–503.
- 321 15. Hoffman BL, Felter EM, Chu K-H, Shensa A, Hermann C, Wolynn T, et al. It's not all about  
322 autism: The emerging landscape of anti-vaccination sentiment on Facebook. *Vaccine.* 2019  
323 10;37(16):2216–23.
- 324 16. Urgent health challenges for the next decade [Internet]. [cited 2020 May 27]. Available  
325 from: [https://www.who.int/news-room/photo-story/photo-story-detail/urgent-health-](https://www.who.int/news-room/photo-story/photo-story-detail/urgent-health-challenges-for-the-next-decade)  
326 [challenges-for-the-next-decade](https://www.who.int/news-room/photo-story/photo-story-detail/urgent-health-challenges-for-the-next-decade)
- 327 17. Stahl J-P, Cohen R, Denis F, Gaudelus J, Lery T, Lepetit H, et al. Vaccination against  
328 meningococcus C. vaccinal coverage in the French target population. *Med Mal Infect.* 2013  
329 Feb;43(2):75–80.
- 330 18. Denis F, Cohen R, Stahl J-P, Martinot A, Dury V, Le Danvic M, et al. Papillomavirus  
331 vaccination in France according to 2008 to 2012 Vaccinoscopie® data. *Médecine Mal Infect*  
332 [Internet]. 2014 Jan [cited 2018 Jan 22];44(1):18–24. Available from:  
333 <http://linkinghub.elsevier.com/retrieve/pii/S0399077X13003247>
- 334 19. Kessels SJM, Marshall HS, Watson M, Braunack-Mayer AJ, Reuzel R, Tooher RL. Factors  
335 associated with HPV vaccine uptake in teenage girls: a systematic review. *Vaccine.* 2012 May  
336 21;30(24):3546–56.
- 337 20. Rodriguez SA, Mullen PD, Lopez DM, Savas LS, Fernández ME. Factors associated with  
338 adolescent HPV vaccination in the U.S.: A systematic review of reviews and multilevel  
339 framework to inform intervention development. *Prev Med.* 2020;131:105968.
- 340 21. Newman PA, Logie CH, Lacombe-Duncan A, Baiden P, Tepjan S, Rubincam C, et al.  
341 Parents' uptake of human papillomavirus vaccines for their children: a systematic review and  
342 meta-analysis of observational studies. *BMJ Open.* 2018 20;8(4):e019206.
- 343 22. Browne MW. Asymptotically distribution-free methods for the analysis of covariance  
344 structures. *Br J Math Stat Psychol.* 1984 May;37 ( Pt 1):62–83.
- 345 23. Cohen J. A power primer. *Psychol Bull.* 1992 Jul;112(1):155–9.
- 346 24. Hatcher PhDL, O'Rourke RDPsychN. Step-by-Step Approach to Using SAS for Factor  
347 Analysis and Structural Equation Modeling, Second Edition, 2nd Edition [Internet]. Place of  
348 publication not identified: SAS Institute; 2013 [cited 2020 Nov 21]. Available from:  
349 <https://www.safaribooksonline.com/library/view/title/9781599942308/?ar?orpq&email=^u>
- 350 25. Gautier A, Verger P, Jestin C et le groupe Baromètre santé 2016. Sources d'information,  
351 opinions et pratiques des parents en matière de vaccination en France en 2016. *Bull Epidémiol*



352 HebdHors-Sér Vaccin. 2017;28–35.

353 26. Dib F, Mayaud P, Launay O, Chauvin P, FSQD-HPVH Study Group. Design and content  
354 validation of a survey questionnaire assessing the determinants of human papillomavirus (HPV)  
355 vaccine hesitancy in France: A reactive Delphi study. *Vaccine*. 2020 Sep 3;38(39):6127–40.

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## 357 **Tables**

358 **Table 1.** Distribution of study variables among 1949 vaccine-hesitant mothers (Vaccinoscopie®  
359 Survey 2015 to 2018).

360 **Table 2.** Results of bivariate and multivariate logistic regression analysis exploring the factors  
361 associated with HPV vaccination (weighted data).

362 **Table 3.** Total, direct, and indirect effects of the Internet and other sources of information on  
363 HPV vaccine uptake (weighted data).

364 **Supplementary table.** Total, direct, and indirect effects of variables other than sources of  
365 information on HPV vaccine uptake (weighted data).

## 366 **Figures**

367 **Figure 1.** Conceptual model with the hypothesized interrelationships between the variables.

368 **Figure 2.** Final model of associations with standardized path coefficients.

369

370 **Author's contributions**

371 FD and PC had designed the study. FD had performed the data analysis, the redaction of the  
372 manuscript, and the revision process of this paper based on Vaccinoscopie Survey data  
373 acquired by OL. PC, OL, PM and LL have participated in the revision process and the redaction of  
374 the manuscript. GSK and IDM had no role in the study design nor in the data analysis. All  
375 authors have approved the final manuscript which was reviewed by GSK before submission.

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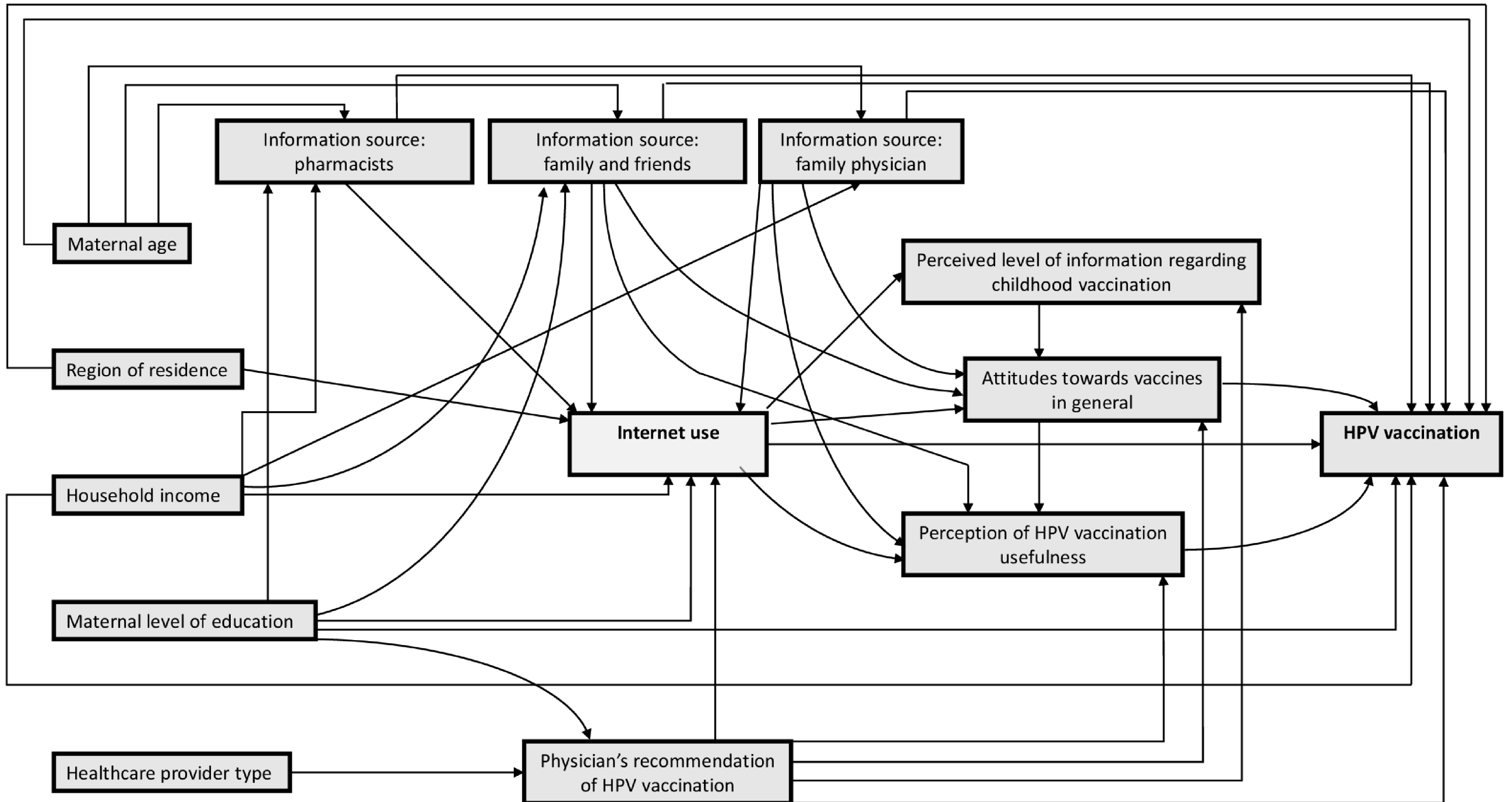
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379 **Conflict of interest**

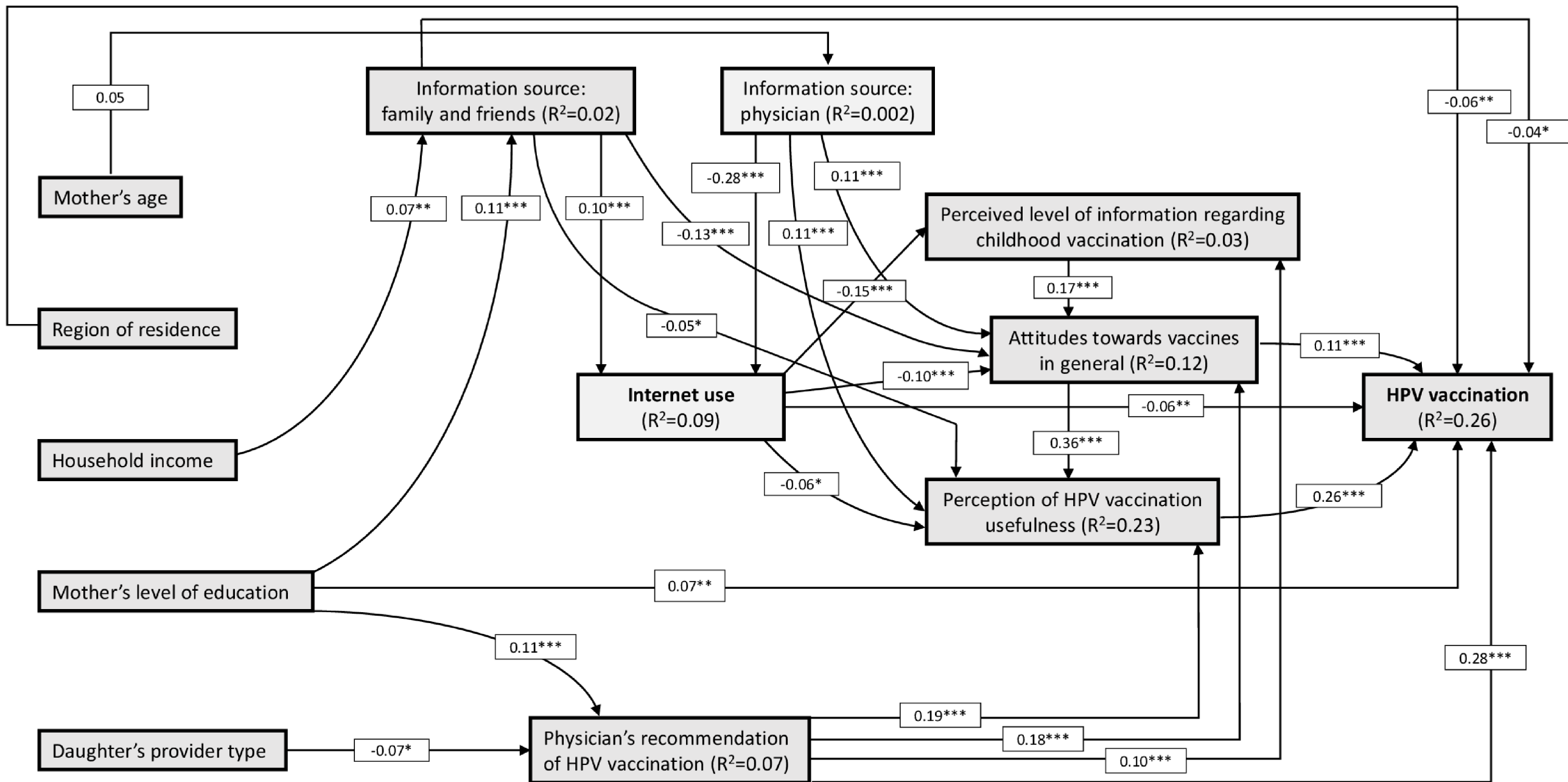
380 FD declares that MSD vaccines have covered registration fees, transport and accommodation  
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**Figure 1:** Conceptual model with the hypothesized interrelationships between the variables.



**Figure 2.** Final model of associations with standardised path coefficients.

Note: standardized path coefficients are presented on the arrows;  $R^2$ = squared multiple correlation (explained variance). \* $p < 0.05$ , \*\* $p < 0.01$ , \*\*\*  $p < 0.0001$

**Table1.** Distribution of study variables among 1949 vaccine hesitant mothers (Vaccinoscope® Survey 2015 to 2018).

	Unweighted data		Weighted data	
	Total		Total	
	(N=1949)		(N=1835)	
	n or mean	(% or SD)	n or mean	(% or SD)
<b>Demographics</b>				
Maternal age (years) <sup>a</sup>	43.3	(4.9)	43.5	(4.9)
Monthly household income (Euros) <sup>b</sup>				
<1700	323	(16.9%)	311	(17.3%)
[1700-2700]	660	(34.5%)	625	(34.7%)
>2700	930	(48.6%)	865	(48.0%)
<b>Educational attainment</b>				
Below high school diploma	395	(20.3%)	379	(20.7%)
High school diploma – two-year post high school diploma	961	(49.3%)	911	(49.6%)
Beyond two-year post high school diploma	593	(30.4%)	545	(29.7%)
<b>Geographic region of residence</b>				
Greater Paris area	319	(16.4%)	295	(16.1%)
Ile de France	330	(16.9%)	362	(19.7%)
Center-East	275	(14.1%)	238	(13.0%)
East	169	(8.7%)	156.6	(8.5%)
North	141	(7.2%)	126	(6.9%)
West	304	(15.6%)	247	(13.5%)
South-West	206	(10.6%)	182	(9.9%)
Mediterranean	205	(10.5%)	229	(12.5%)
<b>Attitudes towards vaccines in general</b>				
In favor of vaccinating against all serious diseases if there are vaccines	1315	(67.5%)	1234	(67.2%)
In favor of minimizing the number of vaccinations	608	(31.2%)	574	(31.3%)
Opposed to all vaccines	9	(0.5%)	9	(0.5%)
No opinion	17	(0.9%)	18	(0.9%)
<b>Perception of HPV vaccination usefulness</b>				
Indispensable	697	(35.8%)	651	(35.5%)
Useful	622	(31.9%)	589	(32.1%)
Not very useful	244	(12.5%)	230	(12.5%)
Useless	140	(7.2%)	135	(7.4%)
Does not know	246	(12.6%)	229	(12.5%)
<b>Physician' recommendation of HPV vaccination</b>				
Yes	1282	(65.8%)	1199	(65.3%)
No	566	(29.0%)	537	(29.3%)
Does not remember	101	(5.2%)	98	(5.3%)
<b>Perceived level of information regarding childhood vaccination</b>				
Not at all well-informed	32	(1.6%)	30	(1.7%)
Rather not well- informed	280	(14.4%)	267	(14.6%)
Rather well-informed	1347	(69.1%)	1266	(69%)
Fully informed	290	(14.9%)	271	(14.8%)
<b>Information sources</b>				
Internet	466	(23.9)	439	(23.9)
Family physician	1789	(91.8)	1686	(91.8)
Pharmacist	283	(14.5%)	273	(14.9%)
Relatives/family/friends	508	(26.1%)	479	(26.1%)
Other	71	(3.6%)	66	(3.6%)
<b>Daughter's healthcare provider type</b>				
Free preventive clinic for mothers and infants	7	(0.4%)	8	(0.4%)
General practice	1790	(91.8%)	1687	(91.9%)
Pediatrician practice	152	(7.8%)	140	(7.6%)
<b>HPV vaccination status</b>				

At least one dose	552	(28.3%)	509	(27.7%)
Not vaccinated	1397	(71.7%)	1327	(72.3%)

Abbreviations: HPV, human papillomavirus

<sup>a</sup> 4 missing values

<sup>b</sup> 36 missing values

	Vaccinated daughters (N=508)		Unvaccinated daughters (N=1327)		Crude OR	95% CI	Adjusted OR *	95% CI
	n or mean	(% or SD)	n	(% or SD)				
<b>Vaccinoscopie® Survey year</b>								
2018	159	(33.1)	321	(66.9)	Ref.			
2017	136	(30.3)	314	(69.7)	0.88	0.67-1.16	1.00	0.71-1.41
2016	107	(23.5)	350	(76.5)	0.62	0.46-0.83	0.64	0.45-0.91
2015	106	(23.7)	342	(76.3)	0.63	0.47-0.84	0.66	0.46-0.94
<b>Demographics</b>								
<i>Maternal age (years) <sup>a</sup></i>	43.6	(4.6)	43.5	(5.0)	1.00	0.98-1.02	-	-
<i>Household income (Euros per month) <sup>b</sup></i>								
<1700	74	(23.7)	238	(76.3)	Ref.			
[1700-2700]	177	(28.3)	448	(71.7)	1.27	0.93-1.74	-	-
>2700	250	(28.9)	615	(71.1)	1.31	0.97-1.77	-	-
<i>Educational attainment</i>								
Below high school diploma	78	(20.5)	301	(79.5)	Ref.			
High school diploma – two-year post high school diploma	251	(27.6)	660	(72.4)	1.47	1.10-1.96	1.40	0.99-1.98
Beyond two-year post high school diploma	179	(32.9)	366	(67.1)	1.90	1.40-2.58	1.81	1.24-2.64
<i>Geographic region of residence</i>								
Regions other than Ile de France	424	28.8	1049	71.2	Ref.			
Ile de France	84	23.3	278	76.7	0.75	0.57-0.98	0.76	0.55-1.04
<b>Attitudes towards vaccines in general</b>								
In favor of minimizing the number of vaccinations or opposed to all vaccines or no opinion	55	(9.2)	546	(90.8)	Ref.			
In favor of vaccinating against all serious diseases if there are vaccines	453	(36.7)	781	(63.3)	5.70	4.23-7.69	2.34	1.64-3.33
<b>Perception of HPV vaccination usefulness</b>								
No very useful or useless or no opinion	12	(2.1)	582	(97.9)	Ref.			
Useful or indispensable	496	(40.0)	745	(60.0)	31.62	17.76-56.29	19.65	10.36-37.24
<b>Physician's recommendation of HPV vaccination</b>								
No or does not remember	27	(4.3)	609	(95.7)	Ref.			
Yes	481	(40.1)	718	(59.9)	15.04	10.06-22.46	10.40	6.85-15.80
<b>Perceived level of information regarding childhood vaccination</b>								
Rather not well or not at all well-informed	51	(17.2)	247	(82.8)	Ref.			

Rather well or fully informed	457	(29.8)	1080	(70.2)	2.04	1.48-2.81	-	-
<b>Information sources</b>								
Family physician								
No	15	(10.4)	134	(89.6)	Ref.			
Yes	493	(29.3)	1193	(70.7)	3.55	2.08-6.07	-	-
Pharmacist								
No	429	(27.5)	1133	(72.5)	Ref.			
Yes	79	(29.1)	194	(70.9)	1.09	0.82 -1.44	-	-
Relatives/family/friends								
No	407	(30.0)	949	(70.0)	Ref.			
Yes	101	(21.2)	378	(78.8)	0.63	0.49-0.80	0.75	0.55-1.01
Internet								
No	429	(30.8)	967	(69.2)	Ref.			
Yes	79	(18.0)	360	(82.0)	0.49	0.38-0.65	0.66	0.47-0.91
<b>Healthcare provider type</b>								
Pediatrician practice or free preventive clinic for mothers and infants	50	(34.2)	98	(65.8)	Ref.			
General practice	458	(27.1)	1229	(72.9)	0.72	0.50-1.02	-	-

Abbreviations: CI, confidence interval; HPV, human papillomavirus; OR, odds ratio; Ref., reference category for odds ratio, SD, standard deviation.

<sup>a</sup> 4 missing values.

<sup>b</sup> 36 missing values.

\* Adjusted odds ratio determined by backward multivariate logistic regression of HPV vaccination.



**Table 3.** Total, direct, and indirect effects of Internet and other sources of information on HPV vaccine uptake (weighted data).

	Total effect		Direct effect		Indirect effect	
	Standardized $\beta$ estimate (standard error)	P value	Standardized $\beta$ estimate (standard error)	P value	Standardized $\beta$ estimate (standard error)	P value
<b>Information source</b>						
Internet	-0.10 (0.02)	<0.0001	-0.06 (0.02)	0.002	-0.04 (0.008)	<0.0001
Family physician	0.08 (0.01)	<0.0001	0	-	0.08 (0.01)	<0.0001
Relatives/family/Friends	-0.09 (0.02)	<0.0001	-0.04 (0.02)	0.033	-0.05(0.007)	<0.0001

**Supplementary table.** Total, direct, and indirect effects of variables other than sources of information on HPV vaccine uptake (weighted data).

	Total effect		Direct effect		Indirect effect	
	Standardized $\beta$ estimate (standard error)	P value	Standardized $\beta$ estimate (standard error)	P value	Standardized $\beta$ estimate (standard error)	P value
Perceived level of information of childhood vaccination	0.03 (0.01)	<0.0001	0	-	0.03(0.01)	<0.0001
Attitudes towards vaccines in general	0.20 (0.02)	<0.0001	0.11 (0.02)	<0.0001	0.09 (0.01)	<0.0001
Perception of HPV vaccine usefulness	0.26 (0.01)	<0.0001	0.26 (0.01)	<0.0001	0	-
Physician recommendation of HPV vaccination	0.37 (0.01)	<0.0001	0.28 (0.01)	<0.0001	0.09 (0.008)	<0.0001
Healthcare provider type	-0.02 (0.01)	0.001	0	-	-0.02 (0.01)	0.001
Geographic region of residence	-0.06 (0.02)	0.002	-0.06 (0.02)	0.002	0	-
Household income	-0.006 (0.002)	0.013	0	-	-0.006 (0.002)	0.013
Maternal age	0.004 (0.002)	0.054	0	-	0.004 (0.002)	0.054
Maternal level of education	0.10 (0.02)	<0.0001	0.07(0.02)	0.001	0.03 (0.01)	0.001