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Optimising HPV vaccination communication to adolescents: A discrete choice experiment

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ABSTRACT

Background: Human Papillomavirus (HPV) vaccine coverage in France is below 30%, despite proven effectiveness against HPV infections and (pre-)cancerous cervical lesions. To optimise vaccine promotion among adolescents, we used a discrete choice experiment (DCE) to identify optimal statements regarding a vaccination programme, including vaccine characteristics.
Methods: Girls and boys enrolled in the last two years of five middle schools in three French regions (aged 13–15 years) participated in an in-class cross-sectional self-administered internet-based study. In ten hypothetical scenarios, participants decided for or against signing up for a school-based vaccination campaign against an unnamed disease. Scenarios included different levels of four attributes: the type of vaccine-preventable disease, communication on vaccine safety, potential for indirect protection, and information on vaccine uptake among peers. One scenario was repeated with an added mention of sexual transmission.
Results: The 1,458 participating adolescents (estimated response rate: 89.4%) theoretically accepted vaccination in 80.1% of scenarios. All attributes significantly impacted theoretical vaccine acceptance. Compared to a febrile respiratory disease, protection against cancer was motivating (odds ratio (OR) 1.29 [95%-CI 1.09–1.52]), but not against genital warts (OR 0.91 [0.78–1.06]). Compared to risk negation ("vaccine does not provoke serious side effects"), a reference to a positive benefit-risk balance despite a confirmed side effect was strongly dissuasive (OR 0.30 [0.24–0.36]), while reference to ongoing international pharmacovigilance without any scientifically confirmed effect was not significantly dissuasive (OR 0.86 [0.71–1.04]). The potential for indirect protection motivated acceptance among girls but not boys (potential for eliminating the disease compared to no indirect protection, OR 1.57 [1.25–1.96]).

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Compared to mentioning "insufficient coverage", reporting that ">80% of young people in other countries got vaccinated" motivated vaccine acceptance (OR 1.94 [1.61–2.35]). The notion of sexual transmission did not influence acceptance.

Conclusion: HPV vaccine communication to adolescents can be tailored to optimise the impact of promotion efforts.

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1. Introduction

Human papillomavirus (HPV) infection is responsible for several cancers [1], including cervical cancer (CC). In France, about 3,000 new cases of CC and 1,117 deaths occurred in 2018 [2], which placed it in 11th position in terms of frequency and 10th in terms of mortality rate in women in 2015 [3].

HPV vaccination effectively prevents HPV infections and (pre-) cancerous cervical lesions [4,5] and has been recommended for girls in France for over ten years. The current recommendation targets girls aged 11–14 years (with a catch-up up to 19 years) and will be expanded to boys starting 2021 [6]. The vaccine coverage in France for 16-year-old girls has remained continuously below 30% [7], among the lowest in Europe [8,9] and represents hundreds of deaths and thousands of infections which could be avoided [10]. Lack of information, concerns about vaccine safety and mistrust in health authorities and new vaccines have been described as the principal barriers [11,12]. French studies also suggested that lack of general practitioners (GP) recommendation and perceived low effectiveness by parents play an important role [13–15]. Previous works using discrete choice experiments (DCE) have underlined the importance of social conformism and indirect protection effects as factors of vaccine acceptance in general [16–18].

In France, HPV vaccines are accessible mainly through private medical practices and gynaecologist consultations, but also through family planning and vaccination centres. The national health insurance covers 65% of the HPV vaccine cost, and the remaining 35% are reimbursed by complementary (private or collective) insurance schemes, which cover about 95% of the French population (but < 90% of the lowest-income households)[19]. School-based HPV vaccination, which in the UK [20] or Australia [21] helped achieve around 90% coverage, occurs only in few French administrative areas.

In this context, the PrevHPV project was designed to develop, implement and evaluate a complex intervention targeting adolescents, parents and GPs. The intervention includes a school-based education programme on HPV vaccination, a school-based vaccination campaign and a GPs motivational interviewing training.

Given the complexity of the determinants of vaccine hesitancy, the World Health Organisation (WHO) recommends the use of social marketing practices to address this issue in specific population groups [22]. Conjoint experiments, and in particular discrete choice experiments (DCEs), have been increasingly used to explore users' healthcare preferences, especially regarding preventive interventions [23–25]. These methods, arising from economics and mathematical psychology, allow assessing the individual and combined impact of a set of factors on a theoretical decision [26], such as choosing between two alternative treatments, or deciding whether or not to opt-in for a preventative programme (e.g., screening or vaccination). This approach thus helps to translate observational evidence into interventions and pre-testing them before implementation. Previous DCEs have studied girls' preferences on HPV vaccine characteristics such as degree/duration of protection, administration route, number of required doses, price and age at vaccination [27–29]. More recently, DCEs were used to document, among other factors, the importance of social conformism, risk of side effects, and herd immunity as factors of vaccine acceptance among university students in France [16] or parents in Belgium [17]. However, they have not been used to inform on adolescents' preferences regarding the content of information campaigns, which would be needed to tailor communication to adolescents' preferences.

As part of the PrevHPV project, we aimed to assess which statements around HPV vaccination had optimal effect on theoretical vaccine acceptance among adolescents to tailor the school-based communication, using a single profile discrete choice experiment (DCE) with opt-out.

2. Methods

2.1. Study design and participant inclusion

We conducted a cross-sectional study from January 31th to March 13th 2020 in five middle schools ("*collège*", **Supplementary File A**) located in three French regions (Grand Est, Pays de la Loire and Auvergne-Rhône-Alpes). The study population were female and male adolescents enrolled in their last two years of middle school (typically aged 13–15 years, corresponding to grades 8 and 9 in the US educational system) in public or private schools. We focused on this age range because younger adolescents are less likely to be involved in vaccine decisions, may find DCE tasks challenging, and because vaccination and human reproduction are part of those grades' curriculum. We randomly selected middle schools in participating regions and invited them to participate voluntarily. The objective was to include at least 1,000 respondents, 200 per gender and socio-economic strata as recommended in Bridges et al. (2011) [24]. Data collection stopped with school closure in response to the Covid-19 epidemic, but a sufficient sample size had been reached by that time.

Participating middle schools sent study information letters to parents, who could refuse their child's participation. Adolescents received the study information in class and had the possibility to refuse or stop their participation at any time while completing the questionnaire. The self-administered and internet-based questionnaire was hosted on the REDCap (Research Electronic Data Capture) tool [30,31] and completed during class. Data collection was anonymous at all stages, and no information on the health status of respondents was collected. We obtained institutional and ethics approval from Inserm IRB (n°19-642).

2.2. Questionnaire

The 15-minute questionnaire comprised four parts: (i) introductory questions such as age and gender, (ii) basic information on infectious diseases and vaccines along with a brief explanation of each attribute (**Supplementary File B**), (iii) the discrete choice experiment and (iv) detailed questions on participants' characteristics, including attitudes on vaccination.

For the DCE, participants were asked to imagine the following situation: A vaccination campaign would be organised at their school in two weeks, during which free vaccination would be offered by a doctor during an individual consultation. Their parents would already be informed and asked for their consent. Based on one changeable set of information given to them by the school nurse, participants would need to decide whether or not to sign up for getting vaccinated during the campaign (Fig. 1). In other words, the choice task was designed as a single profile DCE format with an opt-out.

2.3. Attributes and levels

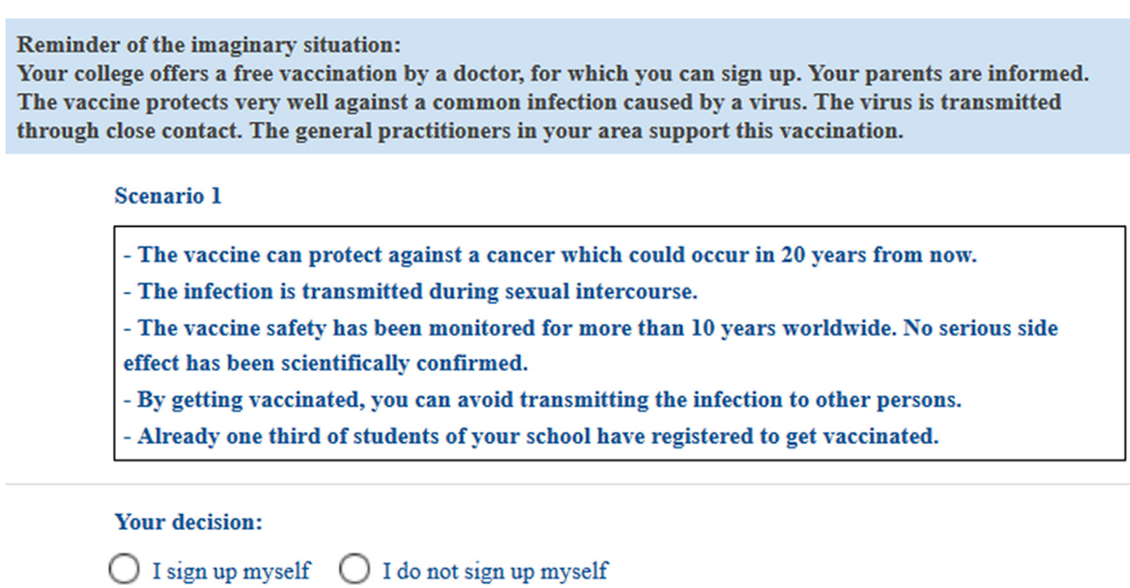
We drafted a first DCE tool version based on a literature review and expert opinion. It aimed to be realistic within a communication campaign in France. This version included barriers and facilitators of vaccine acceptance: disease targeted by the vaccine, vaccine effectiveness, vaccine safety, vaccine access (free, need to consult a doctor), possibility of spacing out cancer screening for girls who got vaccinated, potential for indirect protection, vaccine acceptance rates among peers, vaccine recommendation for girls only or both genders. A panel of eight experts in epidemiology, social psychology, infectious diseases, sociology, and general practice discussed this list of attributes during a consultation meeting. The resulting revised version was reviewed by a health communication specialist to ensure that wording was accessible to lower literacy levels among adolescents. Finally, the questionnaire was tested during five qualitative *think-aloud* interviews [32], during which participants were asked to reflect aloud on their thoughts and feelings when answering the choice tasks. Modifications were made iteratively until saturation was reached (**Supplementary File C**). The final DCE tool included the following hypotheses and attribute (levels) (Table 1).

1) **Disease** (three levels): We hypothesised that mentioning prevention of a cancer that could occur in 20 years (*Cancer in 20 years*) would be less motivating (risk too far in the future) and genital warts (*Genital warts*) would be more motivating than an unnamed febrile respiratory disease (*Respiratory disease*, the reference), because of the imminent discomfort associated with genital warts.
2) **Safety** (four levels): We aimed at evaluating if and to which extent the information about a rare but potentially severe side effect with nevertheless a positive benefit-risk balance – a formulation regularly used by French health authorities (*Benefit-risk*) - would decrease acceptance compared to a straight negation of serious side effects (*No side effects, the reference*). We also hypothesised that factual information about long-standing international surveillance of vaccine safety during which no side effect was scientifically confirmed (*Scientific surveillance*) would increase acceptance compared to the reference. Furthermore, we wanted to test whether explaining that there was no increase in the incidence of side effects that could be due to vaccination in other countries with a high number of vaccinated persons (*Safety other countries*), would increase acceptance compared to the reference (straight negation). Our assumption was that straight negation could amplify mistrust toward authorities and thus vaccination [33].
3) **Indirect Protection** (three levels): Using exclusively individual protection as the reference (*Individual protection only*), we aimed at quantifying by how much acceptance would increase with the information that vaccination blocks the transmission to other persons (*Protects others*), or the potential of disease elimination in case of high coverage (*Elimination*).
4) **Coverage** (four levels): Using the notion of insufficient coverage (*Not enough*) - a formulation frequently used in vaccine communication - as the reference, we aimed to evaluate the extent to which nudging information about low coverage (*Already one third*), or social conformism about high coverage among French adolescents (*Most students*) and in other countries (*Other countries 80%*) could improve acceptance.

To specifically test whether mentioning sexual transmission of the pathogen would decrease acceptance of vaccination among adolescents, we used it as an additional attribute (**Sexual Transmission**, one level), only present in one choice task [34].

2.4. Experimental design

These four attributes provided 128 combinations of attributes' levels in a full factorial design. We used NGENE® software to generate a 36-profile efficient design for a multinomial logit model with non-informative priors for attributes' level parameters and a standard error of 2 for the random model intercept (thus allowing for heterogeneity in stated vaccination uptake). We specified a util-


Reminder of the imaginary situation:
Your college offers a free vaccination by a doctor, for which you can sign up. Your parents are informed. The vaccine protects very well against a common infection caused by a virus. The virus is transmitted through close contact. The general practitioners in your area support this vaccination.

Scenario 1

- The vaccine can protect against a cancer which could occur in 20 years from now.
- The infection is transmitted during sexual intercourse.
- The vaccine safety has been monitored for more than 10 years worldwide. No serious side effect has been scientifically confirmed.
- By getting vaccinated, you can avoid transmitting the infection to other persons.
- Already one third of students of your school have registered to get vaccinated.

Your decision:

○ I sign up myself ○ I do not sign up myself

Fig. 1. Example choice task with the four main attributes and the added transmission attribute.

Table 1
Attributes and levels retained for the discrete choice experiment for a school-based vaccination campaign.

Attributes	Levels (labels)	Levels (short definition)	Assumption to be tested
Disease	Respiratory disease	The vaccine can protect against a disease with high fever and breathlessness.	*Reference*
	Cancer in 20 years	The vaccine can protect against a cancer, which could occur in 20 years from now.	H_1: OR < 1
	Genital warts	The vaccine can protect against genital warts.	H_2: OR > 1
Safety	No side effect	The vaccine does not cause serious side effects.	*Reference*
	Scientific surveillance	The vaccine safety has been monitored for>10 years worldwide. No serious side effect has been scientifically confirmed.	H_3: OR > 1
	Safety other countries	In countries where most adolescents are vaccinated, the risk of a serious side effect that could be due to vaccination has not increased.	H_4: OR > 1
	Benefit/risk	The vaccine can only in rare occasion cause a serious side effect, but the benefit from vaccination are much greater than its risk.	H_5: OR < 1
Indirect Protection	Protects only you	The vaccine protects only you.	*Reference*
	Protects others	By getting vaccinated, you can avoid transmitting the infection to other persons.	H_6: OR > 1
	Elimination	By vaccinating most young people of your age, one can make the disease disappear from the population.	H_7: OR > 1
Coverage	Not enough	Not enough students of your school have registered to get vaccinated.	*Reference*
	Already one third	Already one third of students of your school have registered to get vaccinated.	H_8: OR > 1
	Most students	Most students of your school have registered to get vaccinated (80%).	H_9: OR < 1 if '*free-riding*' OR > 1 if social conformism
	Other countries 80%	In some countries like England and Portugal, >80% of teens are vaccinated.	H_{10}: OR > 1 if social conformism
Transmission (additional attribute)	Transmission	The infection is transmitted during sexual intercourse.	No a priori assumption
Interactions		Protects others*most student	OR < 1 if free-riding
		Elimination*most student	OR < 1 if free-riding

ity function allowing estimation of all main effects and two pre-specified interaction effects (Indirect_*Elimination* * Coverage_*Most-students*; Indirect_*Elimination* * Coverage_*Othercountries80%*) that were judged particularly relevant based on a priori assumption and think-aloud results. This partition was divided into four versions of nine scenarios, or choice tasks, each.

In each version, we then repeated one of the choice tasks with the addition of the Sexual Transmission attribute [34]. Thus, the final design comprised four sets of ten scenarios (40 unique scenarios) randomly assigned to backward or forward order to each respondent (available in **Supplementary File D**).

2.5. Statistical analyses

We described the distribution of participant characteristics and estimated their association with theoretical vaccine acceptance using a full multivariate logistic regression model.

We estimated preference weights for vaccine acceptance using random intercept logit models (through inclusion of a random effect at the respondent level) and expressed as odds ratios for each attribute level [24]. This multi-level analysis allowed for random (unobserved) variation in vaccination acceptance thus accounting for heterogeneity in adolescent's preferences. Because of the panel nature of the data (multiple choices per subject), a fixed (instead of random) effects specification could have been used. Models with the fixed effects specification yielded similar results (Hausman test comparing fixed and random effects specification not significantly different from 0). The main analyses included the four main attributes as independent variables. To explore signals of effect modification by gender, we conducted stratification by gender as well as regressions including interaction terms between attributes and gender.

We calculated average marginal effects to estimate average changes in probability of vaccine acceptance for each attribute level. In a sensitivity analysis, we excluded participants whose decision was uniformly positive or negative (i.e., always accepting or refusing the vaccine in all hypothetical scenarios). Respondents with uniform decisions do not provide any information about their underlying preferences for the attributes of vaccination programmes. Marginal effects can therefore inform on the attribute's impact on vaccine decision either among the overall population or specifically among (hesitant) persons with variable decisions.

Observed determinants of preference heterogeneity were analysed using interaction models (attributes*individual characteristics, variables were included in the final model if they significantly interacted with one or more attributes at the 0.10 level). Finally, to assess the impact of the additional attribute' sexual transmission' on vaccine acceptance, the proportion of adolescents agreeing to vaccinate in the scenario including/excluding this information were compared using equality of proportion tests. All tests were two-tailed. All analyses were conducted on Stata 15 (Stata- Corp LP, College Station, Texas).

3. Results

3.1. Participant characteristics

Among 1,552 respondents (estimated response rate 89.4%), 1,458 participants with valid and complete questionnaires were included (Fig. 2). The mean age of study participants was 13.8 (standard deviation 0.76) years, with 53.4% girls (Table 2). About 40% declared that their mother or father had completed post-secondary education, while about 37% did not know their parents' educational level. One-quarter of participants declared that they also spoke another language than French at home.

Three-quarters of respondents were in favour of vaccination in general, while a large part did not know their immunisation status (between 35.5% for DTaP-IPV and 75.1% for meningococcal C vaccine). Declared HPV immunisation status among girls was 27.2%, with 47.6% being unaware of their status. Over 90% agreed that vaccination was useful and 80% that it could protect others. One third declared being scared of injections, while one quarter was scared of the substances in the vaccine. About half stated that finding trustworthy information on vaccination was easy, while 19.6% found it difficult.

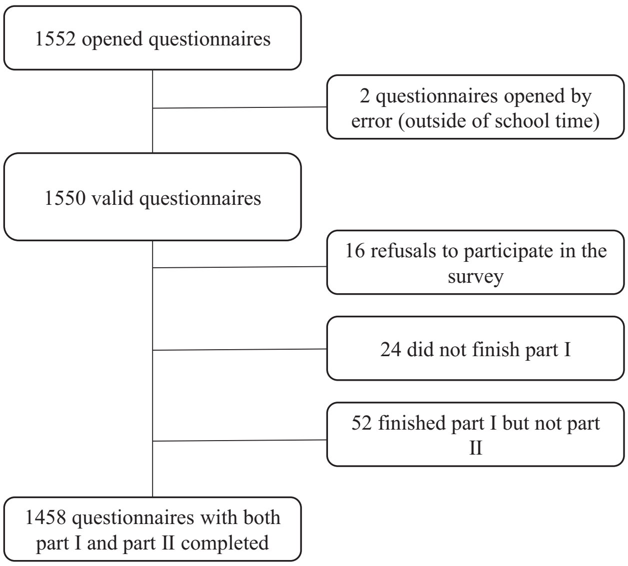


Fig. 2. Flowchart of inclusions.

3.2. Stated preferences

Vaccination was theoretically accepted in 80.1% (range 64.0%-87.7%) of scenarios (**Supplementary File D**). Uniform decisions across all scenarios were made by 51.2% of participants (n = 747), with 6.0% (n = 88) always refusing and 45.2% (n = 659) always accepting vaccination. When removing participants with uniform decisions, vaccination was theoretically accepted in 71.6% of scenarios. Response time was similar for uniform and variable responders (**Supplementary File E**). Theoretical acceptance varied between schools from 66.8% to 84.7%. Individual characteristics significantly associated with theoretical vaccine acceptance were the school, a favourable attitude towards vaccination in general, perceived usefulness of vaccination, only French spoken with parents, stated HPV vaccine status and perceived ease of obtaining trustworthy information (Table 2).

Most attributes and attribute levels contributed significantly to theoretical vaccine decision (Table 3). Other attributes being equal, cancer prevention motivated girls more than the febrile respiratory disease (OR: 1.39, 95%-CI [1.11,1.75]) or genital warts prevention (OR cancer vs warts: 1.37 [1.09,1.73]). This attribute was not statistically significant among boys. Regarding safety, the level "Scientific surveillance" was not significantly different from "No side effect" (OR: 0.86 [0.71–1.04]). Both levels "Safety other countries" and "Benefit/risks" were strongly demotivating (OR: 0.30 [0.24–0.36] for both levels). Any information on indirect protection was motivating for girls (OR for Elimination: 1.57 [1.25;1.96]), but not for boys (OR: 1.19 [0.92;1.55]). Informing on low coverage with a nudge ("already one third") was significantly more motivating than judging it as insufficient (OR 1.48 [1.23;1.78]). Strong social conformism appeared ("most students" OR 1.98 [1.64;2.38] and "other countries 80%" OR 1.94 [1.61–2.35]). No significant difference was found between boys and girls (**Supplementary File F**). We did not find any statistically significant interaction between *Indirect Protection* and *Coverage* attributes in the main sample or by gender (Table 3).

Adding the information on sexual transmission did not significantly influence acceptance (77.8% vs 76.5% acceptance, p = 0.567), with a slight but not significant trend for increased acceptance among boys (Table 4).

We found several significant interactions between attributes and individual characteristics. For example, adolescents agreeing that it is useful to get vaccinated were more sensitive to the mention of "cancer" from the disease attribute (stronger positive effect). For the safety attribute, older adolescents (14 and 15 and older) were less sensitive to the mention of a positive benefit/risk balance compared to younger adolescents (weaker negative effect). Finally, adolescents declaring being "in favour of vaccination" were more sensitive to the high coverage level among their peers or in other countries (stronger positive effect) compared to adolescents declaring not being in favour of vaccination (**Supplementary File G**).

In sensitivity analyses restricted to participants with varying decisions, we found an average 23 percentage point (pp) decrease in the probability of vaccine acceptance with the *Benefit-risk balance* attribute level (8 pp decrease for the overall sample) and a 14 pp increase (5 pp for the overall sample) with information on the high coverage achieved in countries like England and Portugal (Fig. 3 and **Supplementary File H**).

4. Discussion

In this DCE study which evaluated preferences around communication on school-based HPV vaccination among French adolescents, we found that statements on vaccine safety and social conformism had the greatest potential to influence vaccine acceptance in both genders while mentioning the potential for indirect protection and disease elimination had a strong positive impact only among girls. Presenting a low coverage with a nudge was more effective than referring to insufficient coverage. Among girls, prevention of cancer led to a higher acceptance compared to genital warts, while the notion of sexual transmission had no substantial impact in either gender.

The Safety attribute had the strongest negative impact on vaccine acceptance. Vaccine safety doubts are in most populations associated with vaccine hesitancy and mistrust [11,35]. DCE generally investigate this aspect using increasing probabilities of serious side effects [28]. While a French national analysis has described an association of HPV vaccine with Guillain-Barre syndrome [36], WHO considers HPV vaccines as safe given the fact that the French signal could not be scientifically confirmed by reproducing the results in other countries. We investigated how to best communicate on this complex situation. Explaining worldwide surveillance efforts with no scientific confirmation of a serious side effect appears to be most reassuring, while the notion of benefice-risk balance rather emphasised the existence of a severe side effect. Plain negation of serious side effects, used as the reference in our DCE tool, do not appear appropriate as it omits the risk of anaphylactic shock. Strong negation of serious side effects has also been shown to amplify mistrust toward information sources on vaccination [33]. Contrary to our hypothesis that evoking an absence of increased risk in countries with high vaccine coverage would be motivating, it caused similar negative impact as referring to a positive benefit-risk balance despite a severe side effect. It is likely that the wording led respondents to think that the serious side effect was confirmed. Finally, the statement introducing a rare but serious side effect with a maintained positive benefit-risk balance likely should be restricted to scientific considerations and not used in public communication.

Previous studies in France and Belgium [16,37] have described the importance of communicating on high coverage levels while avoiding the notion of "insufficient coverage". The period of adolescence is particularly prone to social conformism [38], which should be integrated into vaccine communication.

Among girls, long-term prevention of a cancer had higher motivating potential than a febrile respiratory disease, which was in opposition with our hypothesis. Harper et al. (2014) investigated decisional satisfaction of women around HPV vaccination and

Table 2
Characteristics of study participants.

Participant characteristics	Total (n = 1458)	Girls (n = 780)	Boys (n = 678)		Association with theoretical vaccine acceptance	
	% in total sample	% among girls	% among boys	p-value for difference*	Odds Ratio **	95%-CI**
Age				0.621		
12 to 13 years old	37.7	37.7	37.8		1	
14 years old	47.1	48	46.2		0.95	[0.71,1.28]
15 to 17 years old	15.2	14.4	16.1		1.12	[0.74,1.70]
Gender				na		
Girl	53.5				1	
Boy	46.5				1.03	[0.76,1.38]
Middle school				0.371		
School 1	8	8.9	6.9		1	
School 2	26.6	26.2	27.1		2.93	[1.69,5.10]
School 3	10.8	11	10.5		1.25	[0.68,2.31]
School 4	28	29	26.8		3.32	[1.94,5.70]
School 5	26.7	25	28.6		2.51	[1.46,4.31]
In favour of vaccination (binary)				0.122		
Disagree or I do not know	23.5	25.1	21.7		1	
Agree or strongly agree	76.5	74.9	78.3		4.81	[3.38,6.82]
In favour of vaccination				0.001	NA	
Strongly agree	30.4	25.6	35.8			
Agree	46.1	49.2	42.5			
I do not know	13.9	15.6	13.9			
Disagree	5.3	5.9	5.3			
Strongly disagree	2.5	3.6	2.5			
Education level of the parents						
Inferior or equal to French baccalaureat	19.2	19.2	19.2	0.279	1	
Superior to French baccalaureat for at least one parent	50.7	49	52.7		0.86	[0.59,1.25]
I do not know, non-applicable	30.1	31.8	28.2		0.84	[0.56,1.25]
Language spoken with parents				0.028		
Only French	75.3	77.6	72.6		1	
Also another language	24.7	22.4	27.4		0.53	[0.38,0.73]
Stated Tdap-IPV vaccine status				0.773		
No	4.3	4	4.7		1	
I do not know	35.5	35.8	35.1		1.00	[0.41,2.40]
Yes	60.2	60.2	60.2		1.22	[0.53,2.82]
Stated MMR vaccine status				0.092		
No	6	4.9	7.3		1	
I do not know	44.6	43.8	45.5		1.30	[0.59,2.86]
Yes	49.4	51.3	47.3		1.47	[0.70,3.08]
Stated MenC vaccine status				<0.001		
No	10.5	8.8	12.6		1	
I do not know	75.1	79.3	70.2		1.02	[0.53,1.99]
Yes	14.4	12	17.2		0.89	[0.44,1.80]
Stated HPV vaccine status				<0.001		
No	24.8	25.3	24.3		1	
I do not know	56	47.6	65.6		1.54	[1.03,2.29]
Yes	19.2	27.2	10.1		1.73	[1.08,2.76]
Stated Hepatitis B vaccine status				0.036		
No	10.3	8.8	12.2		1	
I do not know	64	66.6	60.9		1.45	[0.77,2.74]
Yes	25.7	24.6	27		1.62	[0.86,3.05]
"It is useful to get vaccinated"				0.03		
Disagree	3.2	3.5	3		1	
Agree	91.9	90.4	93.8		3.66	[1.75,7.65]
I do not know	4.8	6.2	3.3		0.85	[0.34,2.15]
"Getting vaccinated can protect others"				0.099		
Disagree	7.2	6.7	7.7		1	
Agree	81.9	80.8	83.2		1.17	[0.69,1.98]
I do not know	10.9	12.5	9.1		0.54	[0.29,1.03]
"Vaccination scares me because of the needle"				<0.001		
Disagree	60.9	51.2	72.2		1	
Agree	34.6	44.7	23.1		0.94	[0.70,1.28]
I do not know	4.4	4.1	4.8		0.70	[0.36,1.35]
"Vaccination scares me because of the substances in the vaccine"				<0.001		
Disagree	64.3	58.9	70.5		1	
Agree	24.3	29.6	18.2		0.93	[0.66,1.30]
I do not know	11.4	11.5	11.3		1.12	[0.72,1.76]
"Do you find it easy to get trustworthy information on vaccination?"				0.063		
Difficult	19.6	21.3	17.6		1	
Easy	52.4	49.6	55.6		1.53	[1.07,2.18]
I do not know	28	29.1	26.8		1.35	[0.91,2.01]

Notes: * p-values obtained from Chi-square test comparing girls and boys on their individual characteristics. ** Odds ratios (OR) and confidence intervals (95%CI) obtained from a full random effect multivariate logit model exploring the associations between theoretical vaccine acceptance and the listed individual characteristics. Tdap-IPV: Tetanus, Diphtheria, Pertussis, Polio; MMR: Measles, Mumps and Rubella; MenC: Meningococcal C; HPV: Human Papillomavirus.

Table 3
Vaccination acceptance in the discrete choice experiment, overall and stratified by gender.

	Overall RE (N = 1458)				Girls RE (N = 780)				Boys RE (N = 678)			
	Main Effect		With interactions		Main Effect		With interactions		Main Effect		With interactions	
Vaccine acceptance	OR	95%-CI	OR	95%-CI	OR	95%-CI	OR	95%-CI	OR	95%-CI	OR	95%-CI
Attributes												
Disease												
Respiratory disease (ref)	1				1				1			
Cancer	1.29	[1.09,1.52]	1.28	[1.07,1.53]	1.39	[1.11,1.75]	1.36	[1.07,1.73]	1.14	[0.88,1.47]	1.14	[0.86,1.51]
Warts	0.91	[0.78,1.06]	0.97	[0.82,1.16]	1.01	[0.83,1.24]	1.10	[0.88,1.38]	0.80	[0.64,1.01]	0.83	[0.63,1.08]
Safety												
No side effect (ref)	1				1				1			
Scientific surveillance	0.86	[0.71,1.04]	0.94	[0.75,1.18]	0.78	[0.60,1.00]	0.85	[0.63,1.16]	0.97	[0.73,1.30]	1.05	[0.75,1.48]
Safety other countries	0.30	[0.24,0.36]	0.31	[0.25,0.38]	0.25	[0.20,0.33]	0.27	[0.20,0.36]	0.35	[0.26,0.47]	0.37	[0.27,0.51]
Benefit/risk	0.30	[0.24,0.36]	0.31	[0.25,0.39]	0.29	[0.22,0.38]	0.31	[0.23,0.41]	0.30	[0.22,0.41]	0.31	[0.23,0.43]
Indirect protection												
Protect only you (ref)	1				1				1			
Protect others	1.30	[1.11,1.52]	1.22	[0.90,1.66]	1.43	[1.16,1.75]	1.31	[0.88,1.95]	1.17	[0.92,1.48]	1.17	[0.72,1.90]
Elimination	1.40	[1.18,1.66]	1.84	[1.29,2.64]	1.57	[1.25,1.96]	2.06	[1.25,3.40]	1.19	[0.92,1.55]	1.59	[0.95,2.67]
Coverage												
Not enough (ref)	1				1				1			
Already one third	1.48	[1.23,1.78]	1.63	[1.18,2.25]	1.56	[1.22,2.00]	1.76	[1.15,2.69]	1.41	[1.06,1.88]	1.53	[0.93,2.54]
Most students	1.98	[1.64,2.38]	2.02	[1.50,2.72]	2.09	[1.62,2.68]	1.87	[1.25,2.78]	1.91	[1.44,2.52]	2.25	[1.43,3.53]
Other countries 80%	1.94	[1.61,2.35]	1.97	[1.44,2.68]	1.81	[1.41,2.33]	1.86	[1.24,2.80]	2.15	[1.60,2.89]	2.21	[1.36,3.61]
Indirect Protection *Coverage												
Protect others*Already one third			0.94	[0.56,1.57]			0.82	[0.42,1.60]			1.06	[0.47,2.37]
Protect others*Most students			1.05	[0.66,1.67]			1.42	[0.76,2.63]			0.75	[0.37,1.53]
Protect others*Other countries 80%			1.29	[0.81,2.06]			1.32	[0.71,2.44]			1.15	[0.56,2.38]
Elimination*Already one third			0.69	[0.40,1.18]			0.76	[0.37,1.57]			0.57	[0.26,1.29]
Elimination*Most students			0.79	[0.49,1.26]			0.86	[0.46,1.64]			0.72	[0.36,1.46]
Elimination*Other countries 80%			0.63	[0.39,1.01]			0.57	[0.30,1.09]			0.68	[0.33,1.38]

RE: random effect specification. OR: Odds ratios. 95%-CI: 95% confidence interval.

Table 4
Probability of acceptance in scenarios with and without the additional attribute of sexual transmission.

	No mention of sexual transmission		Mention of sexual transmission		p-value
Probability of acceptance	%	95%-CI	%	95%-CI	
All	76.5	[73.4,79.6]	77.8	[74.7,80.8]	0.560
Among girls	77.7	[73.6,81.8]	77.0	[72.9,81.2]	0.814
Among boys	74.9	[70.1,79.7]	79.0	[0.74,0.83]	0.257

p-value: two-sample test of proportions.

described greater value in getting vaccinated for cervical cancer prevention compared to genital warts protection [39]. However, Brown et al. (2014), who conducted a DCE on HPV among American girls, found that mentioning protection against genital warts in addition to cancer would be most motivating [29]. By contrast, Wang et al. (2017) found among Australian adolescents that the mention of STI vaccines was only marginally motivating compared to vaccination against a chronic or life-threatening illness [40]. In our study, neither the notion of sexual transmission nor genital warts affected vaccine acceptance significantly. Focusing on cancer prevention instead of sexual health could be more effective and efficient for communication on HPV vaccination.

The motivating role of indirect protection has been described in a previous DCE among French university students [16] but was not found among Australian teenagers [40]. Our results suggest that adolescent girls could be more motivated than boys by arguments calling for altruism or collective engagement although the difference was not statistically significant. This hypothesis is supported by the literature among adults [41,42], althoughamong US male college students, altruistic motives increased vaccine acceptance [43]. More research is needed to better understand the gender-specific aspects of HPV vaccine decision among adolescents and young adults.

Our results suggest that optimised statements on vaccination could increase motivation for vaccination among adolescents. Minors are involved in the vaccine decision-making process [12], and their motivation could also positively impact parental vaccine decisions concerning their children vaccination [44,45]. DCE only address theoretical vaccine acceptance, and the observed effect sizes cannot be readily extrapolated to gains in vaccine coverage, given the complexity of families' vaccine decision and access barriers. However, under the assumption that stated vaccination intentions match actual behaviour, we could approximate that an increase in vaccine coverage between 5 and 15 percentage points could be achieved if a few simple principles were followed when communicating on HPV vaccination during school-based campaigns: avoiding the notion of "insufficient coverage" and communicating instead on high coverage in neighbouring countries; referring to worldwide scientific consensus and efforts to ensure vaccine safety, and to the potential for eliminating cancers caused by HPV.

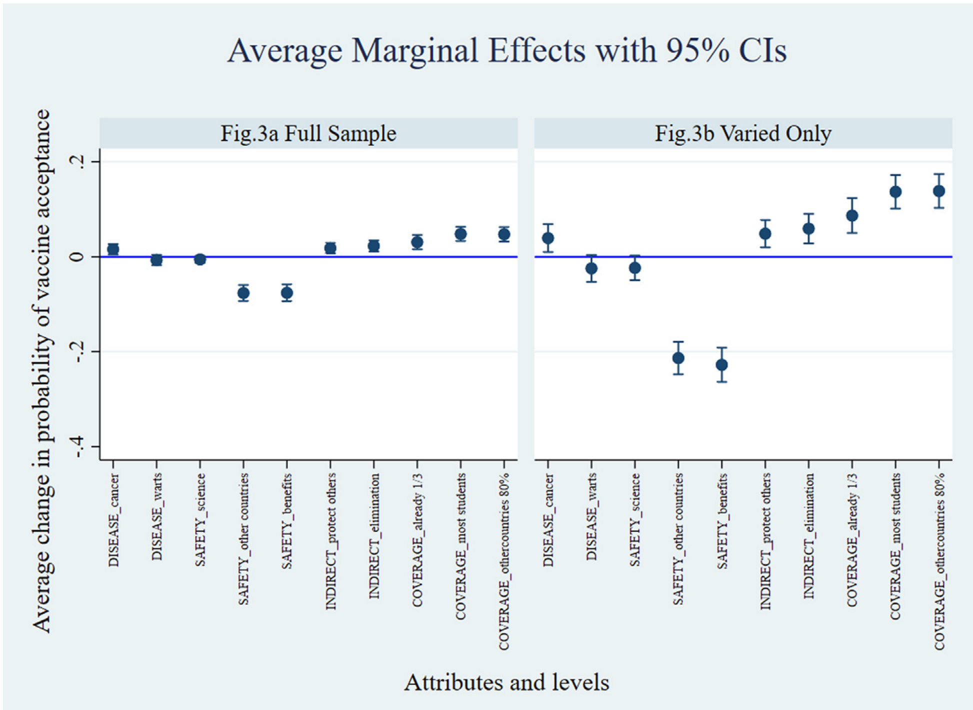


Fig. 3. Average marginal effects of the attribute levels on the probability of vaccine acceptance. 3a: average marginal effects on the full sample (n = 1458). 3b: average marginal effects on the subsample of those who varied in their decision at least once during the experiment (n = 711).

4.1. Study limitations

Our study presents several limitations. First, the prevalence of theoretical vaccine acceptance in our study was high compared to the actual HPV vaccine coverage, an observation already made by a Dutch DCE study [28]. As in all stated preferences studies, interpretation of results must consider the hypothetical nature of decisions. Participants may have chosen to sign up for vaccination knowing that 1) it was a fictional exercise, 2) they could change their mind between the registration and the vaccination campaign, and 3) in real life, the opinion of their parents would have been more important than their own. As our DCE tool did not specify HPV vaccine, participants may have a higher vaccine acceptance than if HPV vaccine had been mentioned. Also, intention is known to represent only 30% of variation in behaviour [46]. However, in our sample, French adolescents were favourable towards vaccination in general, at a similar rate as French adults [47], and the difference between adolescents' preferences and coverage may also be explained by parents' negative opinions on HPV vaccine and/or lack of vaccine recommendation by general practitioners.

Second, our sample is not representative of French adolescents, and no prevalence of attitudes can thus be estimated. However, our sample included a variety of socio-economic settings such that stratified analyses could provide estimations in subgroups. Besides, because of school closure in March 2020 due to the Covid-19 outbreak, we could not include a larger variety of middle schools and geographic regions. Average theoretical vaccine acceptance varied across middle schools, which could be due to uncontrolled local factors, such as a school effect, for example, if students had recently been exposed to training on immunisation or rumours on vaccine safety. Extrapolation beyond our sample and beyond the French context should be made with caution.

Third, although we carefully selected the attributes through a literature review, experts' interviews and think-aloud tests, our experiment is limited to a school-based setting and additional essential attributes may be missing. The fact that about half of participants made (mostly positive) uniform decisions independently of attributes calls for further analysis. Other DCE studies on adolescents described <18% uniform responders [29,48], which could be explained by our objective to inform communication, not to evaluate the impact of extreme constellations (high price, high risk of side effects). This could also be explained by the binary (yes/no) response format, whereas previous studies used pairwise choice tasks with opt-out. Response time was similar for uniform and variable responders, meaning that uniform responders actually provided thoughtful responses. It is thus likely that included attributes did not alter their decision.

5. Conclusion

Our results suggest that appropriate statements on safety profile, referring to high coverage in other countries, cancer prevention (instead of genital warts), potential for protecting others and disease elimination can motivate HPV vaccine acceptance among French adolescents. In a country where HPV vaccine coverage has consistently been below 30%, increasing HPV acceptability is challenging. Statements which could motivate adolescents to get vaccinated thus represent an important tool to rely on in vaccination promotion campaigns. The PrevHPV project will allow testing those statements as part of a school-based interventional study aiming at increasing HPV vaccine coverage, especially with the future extension of HPV vaccine recommendation to boys.

Author contributions

JM, IB, JS and JR conceived the original idea. JM, JS and SC designed the study. FJ, ASDB, AG and SC organised the data collection. SC conducted the analyses and wrote the manuscript under JM and JS's supervision. NT, BG, MM, SB and AG contributed to the data interpretation. All authors revised and approved the manuscript.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.vaccine.2021.05.061.

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