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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 internetbased 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]). 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.

Keywords: HPV, vaccine acceptance, Discrete choice experiment, France, adolescents, communication

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 schoolbased communication, using a single profile discrete choice experiment (DCE) with opt-out.

Methods

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).

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 (Figure 1). In other words, the choice task was designed as a single profile DCE format with an opt-out.

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**).

- Disease (three levels): We hypothesised that mentioning prevention of a cancer that could occur in 20 years (*Cancer in 20 years*) was less motivating (risk too far in the future) and genital warts (*Genital warts*) was 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 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).

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 utility function allowing estimation of all main effects and two pre-specified interaction effects (Indirect_*Elimination* * Coverage_*Moststudents*; 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**).

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 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 indepth stratification by this variable. We conducted further stratified analyses by age group, parental education level and foreign language spoken at home.

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

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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 analyses were conducted on Stata 15 (Stata-Corp LP, College Station, Texas).

Results

Participant characteristics

Among 1,552 respondents (estimated response rate 89.4%), 1,458 participants with valid and complete questionnaires were included (**Figure 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.

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]). Effects were similar in both gender groups. 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**).

When stratifying on individual characteristics, lower and insignificant preference weights for *Elimination* were observed among boys compared to girls, adolescents aged 15-17 years compared to the other age groups, and to a lesser extent, lower parental educational level and the presence of a foreign language spoken at home. However, confidence intervals of subgroups overlapped. (**Figure 3**).

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 F**).

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 (**Figure 4** and **Supplementary File G**).

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. Prevention of cancer led to a higher acceptance among girls than of 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.

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Long-term prevention of a cancer had higher motivating potential among girls than a febrile respiratory disease. Harper et al. (2014) investigated decisional satisfaction of women around HPV vaccination and 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, which is supported by the literature among adults (41,42). However, among US male college students, altruistic motives increased vaccine acceptance (43). More research is needed to understand better 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.

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

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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 fewer than 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.

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.

Competing interests

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

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.

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Supplementary material captions

Supplementary File A - Brief description of middle schools' characteristics

Supplementary File B - Information given before the choice tasks. (authors' translation)

Supplementary File C – Modifications made on the attributes and levels

Supplementary File D - Average percentage of vaccine acceptance for each scenario; from lowest to highest

Supplementary File E – Response Time by Uniform/varied decision

Supplementary File F – Results of random intercept logit models of vaccination acceptance including interactions between attributes and individual characteristics

Supplementary File G – Vaccination acceptance in the "Overall sample" and the "Varied decision only" subsample

References

1. Bansal A, Singh M, Rai B. Human papillomavirus-associated cancers: A growing

global problem. Int J Appl Basic Med Res. 2016;6(2):84.

- Hamers FF, Woronoff A-S, Réseau français des registres de cancers Francim. Cancer du col de l'utérus en France : tendances de l'incidence et de la mortalité jusqu'en 2018. Bull Epidémiol Hebd [Internet]. 2019;22–23:410–6. Available from: http://beh.santepubliquefrance.fr/beh/2019/22-23/2019_22-23_1.html
- Institut national du cancer. Les cancers en France Les données Edition 2015
 [Internet]. Boulogne; 2015. Available from: www.e-cancer.fr
- Garland SM, Kjaer SK, Muñoz N, Block SL, Brown DR, Dinubile MJ, et al. Impact and effectiveness of the quadrivalent human papillomavirus vaccine: A systematic review of 10 years of real-world experience [Internet]. Vol. 63, Clinical Infectious Diseases. 2016 [cited 2020 Apr 20]. p. 519–27. Available from: http://www.ncbi.nlm.nih.gov/pubmed/27230391
- Lei J, Ploner A, Elfström KM, Wang J, Roth A, Fang F, et al. HPV Vaccination and the Risk of Invasive Cervical Cancer. N Engl J Med [Internet]. 2020 Oct 1;383(14):1340– 8. Available from: http://www.nejm.org/doi/10.1056/NEJMoa1917338
- Ministère des Solidarités et de la Santé. Le calendrier des vaccinations 2020 [Internet].
 2020 [cited 2020 Apr 21]. Available from: https://solidarites-sante.gouv.fr/preventionen-sante/preserver-sa-sante/vaccination/calendrier-vaccinal
- Fonteneau L, Barret A-S, Levy Bruhl D. Évolution de la couverture vaccinale du vaccin contre le papillomavirus en France 2008-2018. Bull Epidémiol Hebd. 2019;22–23:424–30.
- 8. Sheikh S, Biundo E, Courcier S, Damm O, Launay O, Maes E, et al. A report on the status of vaccination in Europe. Vol. 36, Vaccine. Elsevier Ltd; 2018. p. 4979–92.

- Nguyen-Huu N-H, Thilly N, Derrough T, Sdona E, Claudot F, Pulcini C, et al. Human papillomavirus vaccination coverage, policies, and practical implementation across Europe. Vaccine [Internet]. 2020 Feb;38(6):1315–31. Available from: https://doi.org/10.1016/j.vaccine.2019.11.081
- Uhart M, Adam M, Dahlab A, Bresse X. Loss of chance associated with sub-optimal HPV vaccination coverage rate in France. Papillomavirus Res. 2017 Jun 1;3:73–9.
- Karafillakis E, Simas C, Jarrett C, Verger P, Peretti-Watel P, Dib F, et al. HPV vaccination in a context of public mistrust and uncertainty: a systematic literature review of determinants of HPV vaccine hesitancy in Europe. Hum Vaccines Immunother. 2019 Aug 3;15(7–8):1615–27.
- Gowda C, Schaffer SE, Dombkowski KJ, Dempsey AF. Understanding attitudes toward adolescent vaccination and the decision-making dynamic among adolescents, parents and providers. BMC Public Health. 2012 Jul 7;12(1):1–10.
- Amessi L. Connaissances sur les infections génitales à HPV et couverture vaccinale HPV des élèves d'un collège à Paris. 2016.
- Ecollan M. Connaissances et facteurs associés à la vaccination anti-HPV chez les parents des élèves de deux collèges parisiens. 2016.
- 15. Verrier F, Gautier A, Quelet S, Bonmarin I. Human papillomavirus infections: influence of perceptions of disease and vaccine on immunization status. Bull Epidémiol Hebd [Internet]. 2019;(22/23):450–6. Available from: http://beh.santepubliquefrance.fr/beh/2019/22-23/pdf/2019_22-23_6.pdf
- Seanehia J, Treibich C, Holmberg C, Müller-Nordhorn J, Casin V, Raude J, et al.Quantifying population preferences around vaccination against severe but rare diseases:

A conjoint analysis among French university students, 2016. Vaccine [Internet]. 2017 May;35(20):2676–84. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0264410X17304383

17. Verelst F, Willem L, Kessels R, Beutels P. Individual decisions to vaccinate one's child or oneself: A discrete choice experiment rejecting free-riding motives. Soc Sci Med [Internet]. 2018 Jun;207(May):106–16. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0277953618302053

- Verelst F, Kessels R, Delva W, Beutels P, Willem L. Drivers of vaccine decisionmaking in South Africa: A discrete choice experiment. Vaccine [Internet]. 2019 Apr;37(15):2079–89. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0264410X19302634
- 19. Perronnin M, Louvel A. La complémentaire santé en 2014 : 5 % de non-couverts et 12 % parmi les 20 % les plus pauvres. Quest d'économie la santé [Internet]. 2018;229:1–
 6. Available from: http://www.irdes.fr/recherche/questions-d-economie-de-la-sante/229-la- complementaire-sante-en-2014.pdf
- 20. Sinka K, Kavanagh K, Gordon R, Love J, Potts A, Donaghy M, et al. Achieving high and equitable coverage of adolescent HPV vaccine in Scotland. J Epidemiol Community Health [Internet]. 2014 [cited 2020 Aug 21];68(1):57–63. Available from: https://pubmed.ncbi.nlm.nih.gov/23986492/
- 21. Patel C, Brotherton JML, Pillsbury A, Jayasinghe S, Donovan B, Macartney K, et al. The impact of 10 years of human papillomavirus (HPV) vaccination in Australia: What additional disease burden will a nonavalent vaccine prevent? Eurosurveillance. 2018;23(41):30–40.
- 22. Nowak GJ, Gellin BG, MacDonald NE, Butler R, Eskola J, Liang X, et al. Addressing

vaccine hesitancy: The potential value of commercial and social marketing principles and practices. Vaccine. 2015;33(34):4204–11.

- 23. de Bekker-Grob EW, Ryan M, Gerard K. Discrete choice experiments in health economics: a review of the literature. Health Econ [Internet]. 2012 Feb [cited 2020 May 5];21(2):145–72. Available from: http://doi.wiley.com/10.1002/hec.1697
- 24. Bridges JFP, Hauber AB, Marshall D, Lloyd A, Prosser LA, Regier DA, et al. Conjoint Analysis Applications in Health—a Checklist: A Report of the ISPOR Good Research Practices for Conjoint Analysis Task Force. Value Heal [Internet]. 2011 Jun;14(4):403–13. Available from: https://linkinghub.elsevier.com/retrieve/pii/S1098301510000835
- 25. Soekhai V, de Bekker-Grob EW, Ellis AR, Vass CM. Discrete Choice Experiments in Health Economics: Past, Present and Future. Pharmacoeconomics [Internet]. 2019 Feb 13 [cited 2020 Jul 30];37(2):201–26. Available from: https://pubmed.ncbi.nlm.nih.gov/30392040/
- 26. Ryan M. Using conjoint analysis to take account of patient preferences and go beyond health outcomes: An application to in vitro fertilisation. Soc Sci Med [Internet]. 1999
 Feb [cited 2020 May 5];48(4):535–46. Available from: http://www.ncbi.nlm.nih.gov/pubmed/10075178
- 27. Hofman R, De Bekker-Grob EW, Richardus JH, De Koning HJ, Van Ballegooijen M, Korfage IJ. Have preferences of girls changed almost 3 years after the much debated start of the HPV vaccination program in the Netherlands? A discrete choice experiment. PLoS One. 2014;9(8).
- de Bekker-Grob EW, Hofman R, Donkers B, van Ballegooijen M, Helmerhorst TJMM,
 Raat H, et al. Girls' preferences for HPV vaccination: A discrete choice experiment.

Vaccine [Internet]. 2010;28(41):6692–7. Available from: http://dx.doi.org/10.1016/j.vaccine.2010.08.001

- Brown DS, Poulos C, Johnson FR, Chamiec-Case L, Messonnier ML. Adolescent Girls' Preferences for HPV Vaccines: A Discrete Choice Experiment. In: Preference Measurement in Health (Advances in Health Economics and Health Services Research) [Internet]. Emerald Group Publishing Limited; 2014. p. 93–121. Available from: https://www.emerald.com/insight/content/doi/10.1108/S0731-219920140000024002/full/html
- 30. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)-A metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform. 2009 Apr 1;42(2):377–81.
- Harris PA, Taylor R, Minor BL, Elliott V, Fernandez M, O'Neal L, et al. The REDCap consortium: Building an international community of software platform partners. Vol. 95, Journal of Biomedical Informatics. Academic Press Inc.; 2019. p. 103208.
- Ryan M, Watson V, Entwistle V. Rationalising the "irrational": A think aloud study of discrete choice experiment responses. Health Econ [Internet]. 2009 [cited 2020 Aug 18];18(3):321–36. Available from: https://pubmed.ncbi.nlm.nih.gov/18651601/
- Betsch C, Sachse K. Debunking vaccination myths: Strong risk negations can increase perceived vaccination risks. Heal Psychol [Internet]. 2013 [cited 2015 Sep 1];32(2):146–55. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22409264
- 34. Mansfield C, Sutphin J, Boeri M. Assessing the impact of excluded attributes on choice in a discrete choice experiment using a follow-up question. Health Econ [Internet].
 2020 Jul 6 [cited 2020 Aug 18];hec.4124. Available from:

https://onlinelibrary.wiley.com/doi/abs/10.1002/hec.4124

- 35. Karafillakis E, Larson HJ. The benefit of the doubt or doubts over benefits? A systematic literature review of perceived risks of vaccines in European populations. Vaccine [Internet]. 2017;35(37):4840–50. Available from: http://dx.doi.org/10.1016/j.vaccine.2017.07.061
- 36. Miranda S, Chaignot C, Hristophe, Collin C, Dray-Spira R, Weill A, et al. Human papillomavirus vaccination and risk of autoimmune diseases: A large cohort study of over 2million young girls in France. Vaccine [Internet]. 2017 Aug 24 [cited 2020 Apr 30];35(36):4761–8. Available from: http://www.ncbi.nlm.nih.gov/pubmed/28750853
- 37. Godinot LD, Sicsic J, Lachâtre M, Abiteboul D, Rouveix E, Raude J, et al. Quantifying preferences around vaccination against frequent, mild disease with risk for vulnerable persons: A discrete choice experiment among French hospital health care workers [Internet]. 2020 Nov [cited 2020 Nov 23]. Available from: https://halshs.archivesouvertes.fr/halshs-03008549
- 38. Dayan J, Guillery-Girard B. Conduites adolescentes et développement cérébral : psychanalyse et neurosciences. Adolescence [Internet]. 2011;77(3):479. Available from: https://www.cairn-int.info/load_pdf.php?ID_ARTICLE=E_ADO_077_0479
- 39. Harper DM, Irons BB, Alexander NM, Comes JC, Smith MS, Heutinck MA, et al.
 Quantifying the decisional satisfaction to accept or reject the human papillomavirus (HPV) vaccine: A preference for cervical cancer prevention. PLoS One. 2014 Feb 14;9(2).
- Wang B, Chen G, Ratcliffe J, Afzali HHA, Giles L, Marshall H. Adolescent values for immunisation programs in Australia: A discrete choice experiment. PLoS One [Internet]. 2017;12(7):e0181073. Available from:

https://journals.plos.org/plosone/article/file?id=10.1371/journal.pone.0181073&type=p rintable

- Zarbatany L, Hartmann DP, Gelfand DM, Vinciguerra P. Gender Differences in Altruistic Reputation. Are They Artifactual? Dev Psychol [Internet]. 1985 Jan [cited 2020 Jun 22];21(1):97–101. Available from: /record/1985-14218-001
- Braaas-Garza P, Capraro V, Rascon E. Gender Differences in Altruism on Mechanical Turk: Expectations and Actual Behaviour. SSRN Electron J [Internet]. 2018 Jun 23
 [cited 2020 Jun 22]; Available from: https://papers.ssrn.com/abstract=2796221
- 43. Bonafide KE, Vanable PA. Male Human Papillomavirus Vaccine Acceptance Is Enhanced by a Brief Intervention that Emphasises Both Male-Specific Vaccine Benefits and Altruistic Motives. Sex Transm Dis [Internet]. 2015 Feb 2 [cited 2020 Jun 19];42(2):76–80. Available from: http://content.wkhealth.com/linkback/openurl?sid=WKPTLP:landingpage&an=000074

35-201502000-00005

- Berenson AB, Laz TH, Hirth JM, McGrath CJ, Rahman M. Effect of the decisionmaking process in the family on HPV vaccination rates among adolescents 9–17 years of age. Hum Vaccin Immunother [Internet]. 2014 Jul 7;10(7):1807–11. Available from: https://www.tandfonline.com/doi/full/10.4161/hv.28779
- 45. Chang J, Ipp LS, de Roche AM, Catallozzi M, Breitkopf CR, Rosenthal SL.
 Adolescent-Parent Dyad Descriptions of the Decision to Start the HPV Vaccine Series.
 J Pediatr Adolesc Gynecol [Internet]. 2018 Feb;31(1):28–32. Available from: https://linkinghub.elsevier.com/retrieve/pii/S1083318817304771
- 46. Sheeran P. Intention—Behavior Relations: A Conceptual and Empirical Review. Eur Rev Soc Psychol [Internet]. 2002 Jan 1 [cited 2020 Nov 19];12(1):1–36. Available

from: https://www.tandfonline.com/doi/abs/10.1080/14792772143000003

- 47. Gautier A, Chemlal K, Jestin C, le groupe Baromètre santé 2016. Adhésion à la vaccination en France : résultats du Baromètre santé 2016. Bull Epidemiol Hebd. 2017;Hors-série(21–7):339–44.
- 48. Marshall HS, Chen G, Clarke M, Ratcliffe J. Adolescent, parent and societal preferences and willingness to pay for meningococcal B vaccine: A Discrete Choice Experiment. Vaccine [Internet]. 2016 Jan 27 [cited 2020 Jul 10];34(5):671–7. Available from: http://dx.doi.org/10.1016/j.vaccine.2015.11.075

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	The vaccine safety has been monitored for more than 10 years worldwide. No serious side effect	H ₃ : OR>1
	surveillance	has been scientifically confirmed.	
	Safety other countries	In countries where most adolescents are vaccinated, the risk of a serious side effect that could be	H ₄ : OR>1
		due to vaccination has not increased.	
	Benefit/risk	The vaccine can only in rare occasion cause a serious side effect, but the benefit from	H ₅ : OR<1
		vaccination are much greater than its risk.	
Indirect	Protects only you	The vaccine protects only you.	Reference
Protection	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	H ₇ : OR>1
		population.	
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 ' <i>free-riding</i> '
			OR>1 if social conformism
	Other countries 80%	In some countries like England and Portugal, more than 80% of teens are vaccinated.	H ₁₀ : OR>1 if social
			conformism
Transmission	Transmission	The infection is transmitted during sexual intercourse.	No a priori assumption
(additional			
attribute)			
Interactions		Protects others*most student	OR<1 if free-riding
		Elimination*most student	OR<1 if free-riding

						Associat	
						ion with	
		Total	Girls	Boys		theoreti	
	Participant characteristics	(n=14	(n=7	(n=6		cal	
		58)	80)	78)		vaccine	
						accepta	
						nce	
		% in	%	%	p-value		
		total	amon	amon	for	Odds	95%-
		sampl	g	g	differen	Ratio **	CI**
		e	girls	boys	ce*		
Age					0.621		
	12 to 13 years old	37.7	37.7	37.8		1	
	14 years ald	47 1	19	46.2		0.05	[0.71,1.
	14 years old	47.1	40	40.2		0.95	28]
	15 to 17 years old	15.2	14.4	16.1		1 1 2	[0.74,1.
	15 to 17 years old	13.2	14.4	10.1		1.12	70]
Gender					na		
	Girl	53.5				1	
	Pov	16.5				1.03	[0.76,1.
	Ббу	40.5				1.05	38]
Middle	school				0.371		
	School 1	8	8.9	6.9		1	
	School 2	26.6	26.2	27.1		2.03	[1.69,5.
		20.0	26.2	27.1		2.93	10]

Table 2: Characteristics of study participants

0.112	10.0	11	10.5		1.25	[0.68,2.
School 3	10.8	11	10.5		1.25	31]
						[1.94,5.
School 4	28	29	26.8		3.32	70]
						[1 /6 /
School 5	26.7	25	28.6		2.51	[1.40,4.
						31]
In favour of vaccination (binary)				0.122		
Disagree or I do not know	23.5	25.1	21.7		1	
			7 0 2		4.01	[3.38,6.
Agree or strongly agree	76.5	74.9	78.3		4.81	82]
Education level of the parents						
Information on aqual to Enough						
interior or equal to French	19.2	19.2	19.2	0.279	1	
baccalaureat						
Superior to French baccalaureat	50.7	40	52.7		0.86	[0.59,1.
for at least one parent	5017	.,				25]
						[0.56,1.
I do not know, non-applicable	30.1	31.8	28.2		0.84	25]
Language spoken with parents				0.028		
				0.020		
Only French	75.3	77.6	72.6		1	
Also another language	24 7	22.4	27.4		0.53	[0.38,0.
This unotion funguage	21.7	22.1	27.1		0.55	73]
Stated Tdap-IPV vaccine status				0.773		
No	4.3	4	4.7		1	
						[0.41,2.
I do not know	35.5	35.8	35.1		1.00	401
						.0.52.2
Yes	60.2	60.2	60.2		1.22	[0.53,2.
						82]

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	

			<u> </u>			0.44	[1.75,7.
	Agree	91.9	90.4	93.8		3.66	65]
							[0.34,2.
	l do not know	4.8	6.2	3.3		0.85	15]
"Getting	g vaccinated can protect others"				0.099		
	Disagree	7.2	6.7	7.7		1	
	A	01.0	00.0	02.2		1 17	[0.69,1.
	Agree	81.9	80.8	83.2		1.1/	98]
							<u> </u>
	I do not know	10.9	12.5	9.1		0.54	[0.29,1.
							03]
"Vaccin	ation scares me because of the				<0.001		
needle"					<0.001		
	Disagree	60.9	51.2	72.2		1	
	Dibugieo	00.7	0112	, 2:2		•	
	Agree	34.6	44.7	23.1		0.94	[0.70,1.
		0.110					28]
				4.8		0.70	[0.36,1.
	I do not know	4.4	4.1				35]
"Vaccin	ation scares me because of the subs	stances					
in the we	anina''				< 0.001		
In the va	lecine						
	Disagree	64.3	58.9	70.5		1	
			0 0 f	10.0		0.00	[0.66,1.
	Agree	24.3	29.6	18.2		0.93	30]
							[0.72.1
	I do not know	11.4	11.5	11.3		1.12	[0.72,1.
							76]
"Do you	find it easy to get trustworthy info	rmation			0.062		
on vacci	nation?"				0.005		
	Difficult	19.6	21.3	17.6		1	
		->.0	_1.0	- / • •		•	

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 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

	O	verall RE	E (N=	1458)		Girls RE	(N=7	N=780) Boys RE			L (N=678)			
	With					With						With		
	Mai	n Effect	inte	ractions	Mai	n Effect	inte	ractions	Mai	n Effect	inte	ractions		
Vaccine	0	95%-	0	95%-	0	95%-	0	95%-	0	95%-	0	95%-		
acceptance	R	CI	R	CI	R	CI	R	CI	R	CI	R	CI		
Attributes														
Disease														
Respirator														
y disease														
(ref)	1				1				1					
	1.	[1.09,	1.	[1.07,	1.	[1.11,	1.	[1.07,	1.	[0.88,	1.	[0.86,		
Cancer	29	1.52]	28	1.53]	39	1.75]	36	1.73]	14	1.47]	14	1.51]		
	0.	[0.78,	0.	[0.82,	1.	[0.83,	1.	[0.88,	0.	[0.64,	0.	[0.63,		
Warts	91	1.06]	97	1.16]	01	1.24]	10	1.38]	80	1.01]	83	1.08]		
Safety														
No side														
effect (ref)	1				1				1					
Scientific	0.	[0.71,	0.	[0.75,	0.	[0.60,	0.	[0.63,	0.	[0.73,	1.	[0.75,		
surveillance	86	1.04]	94	1.18]	78	1.00]	85	1.16]	97	1.30]	05	1.48]		
Safety														
other	0.	[0.24,	0.	[0.25,	0.	[0.20,	0.	[0.20,	0.	[0.26,	0.	[0.27,		
countries	30	0.36]	31	0.38]	25	0.33]	27	0.36]	35	0.47]	37	0.51]		
Benefit/ris	0.	[0.24,	0.	[0.25,	0.	[0.22,	0.	[0.23,	0.	[0.22,	0.	[0.23,		
k	30	0.36]	31	0.39]	29	0.38]	31	0.41]	30	0.41]	31	0.43]		

Indirect

protection

Protect												
only you												
(ref)	1				1				1			
Protect	1.	[1.11,	1.	[0.90,	1.	[1.16,	1.	[0.88,	1.	[0.92,	1.	[0.72,
others	30	1.52]	22	1.66]	43	1.75]	31	1.95]	17	1.48]	17	1.90]
Eliminatio	1.	[1.18,	1.	[1.29,	1.	[1.25,	2.	[1.25,	1.	[0.92,	1.	[0.95,
n	40	1.66]	84	2.64]	57	1.96]	06	3.40]	19	1.55]	59	2.67]
Coverage												
Not												
enough (ref)	1				1				1			
Already	1.	[1.23,	1.	[1.18,	1.	[1.22,	1.	[1.15,	1.	[1.06,	1.	[0.93,
one third	48	1.78]	63	2.25]	56	2.00]	76	2.69]	41	1.88]	53	2.54]
Most	1.	[1.64,	2.	[1.50,	2.	[1.62,	1.	[1.25,	1.	[1.44,	2.	[1.43,
students	98	2.38]	02	2.72]	09	2.68]	87	2.78]	91	2.52]	25	3.53]
Other												
countries	1.	[1.61,	1.	[1.44,	1.	[1.41,	1.	[1.24,	2.	[1.60,	2.	[1.36,
80%	94	2.35]	97	2.68]	81	2.33]	86	2.80]	15	2.89]	21	3.61]
Indirect												
Protection												
*Coverage												
Protect												
others*Alrea			0.	[0.56,			0.	[0.42,			1.	[0.47,
dy one third			94	1.57]			82	1.60]			06	2.37]

others*Most	1.	[0.66,	1.	[0.76,	0.	[0.37,
students	05	1.67]	42	2.63]	75	1.53]
Protect						
others*Other						
countries	1.	[0.81,	1.	[0.71,	1.	[0.56,
80%	29	2.06]	32	2.44]	15	2.38]
Eliminatio						
n*Already	0.	[0.40,	0.	[0.37,	0.	[0.26,
one third	69	1.18]	76	1.57]	57	1.29]
Eliminatio						
n*Most	0.	[0.49,	0.	[0.46,	0.	[0.36,
students	79	1.26]	86	1.64]	72	1.46]
Eliminatio						
n*Other						
countries	0.	[0.39,	0.	[0.30,	0.	[0.33,
80%	63	1.01]	57	1.09]	68	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 men	tion of sexual	Menti	Mention of sexual			
	tran	smission	trar	smission	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.

Figures

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

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



Figure 2: Flowchart of inclusions



Figure 3: Vaccine acceptance for attribute levels regarding potential for indirect protection. Stratification on gender, age category, education level of the parents, and presence of a foreign language spoken with parents

Example interpretation: Compared to the level "Protects only you", the level "Protects others" has a significant effect on acceptance among girls, but not among boys.



Average Marginal Effects with 95% CIs

Figure 4: Average marginal effects of the attribute levels on the probability of vaccine acceptance. 4a: average marginal effects on the full sample (n=1458). 4b: average marginal effects on the subsample of those who varied in their decision at least once during the experiment (n=711)

Supplementary Files

Supplementary File A – Brief description of middle schools' characteristics

	Public / Private	REP*	Urban / Rural
School 1	Public	Yes	Urban
School 2	Private	No	Urban
School 3	Public	No	Rural
School 4	Public	No	Rural
School 5	Public	No	Urban

*REP or "Réseaux d'éducation prioritaires" means schools located in deprived areas can beneficiate from a specific educational program aiming at reducing social and territorial inequalities.

Supplementary File B - Information given before the choice tasks. (authors' translation) *Complete questionnaire in French available upon request.*

Introduction following the questionnaire (1/5)

In this second part of the questionnaire, we ask you to imagine the following situation:

In your school, you can get vaccinated in a fortnight during an individual consultation with a general practitioner, free of charge. The school nurse will give you information to help you make a decision.

If you want to get vaccinated, you must register for an appointment. Your parents have been informed, and their agreement will be collected separately.

We are going to present you with 10 scenarios that differ in the information given by the nurse. For each scenario, we ask you to decide as you would in real life.

Introduction: Reminder of how vaccines work (2/5)

Our bodies are constantly exposed to various microbes. An infection means that our body is in contact with a germ, such as a virus, which can cause illness.

The body defends itself by making antibodies, substances that recognise and eliminate the microbe. Sometimes the body is not strong enough, and you get sick, or the microbe can stay in your body and cause illness long afterwards.

Vaccination allows the body to produce antibodies before you come into contact with the germ. The body is then ready to defend itself when it comes into contact with the germ.

If our body is infected with a germ, we may pass it on to others around us. Some vaccines, but not all, prevent you from spreading the infection to others. If many people are vaccinated, the germ can no longer infect anyone, and the disease disappears from the population.

Introduction: General description of the proposed vaccination in this imaginary situation (these elements apply to all scenarios) (3/5)

* The vaccination presented is imaginary, so the information does not necessarily correspond to an existing vaccine.

* The vaccine protects against a common infection caused by a virus.

* The virus is transmitted by close contact. Anyone can be infected.

* The virus can also eliminate itself from the body without causing disease but vaccination is the only effective means of protection.

* The vaccine has good effectiveness; it protects against 90% of infections. The protection provided by the vaccine persists into adulthood.

* Like other vaccines, this vaccine may cause temporary effects: pain and redness at the site of the sting, fever, headache, or rare allergic reactions.

* The vaccine has been used in France and many other countries for 10 years or longer.

Introduction: Variable information (4/5)

The 10 scenarios vary according to the following information.

- The disease (consequences of the infection) against which the vaccine protects is either:

* An illness with a high fever and difficulty breathing, which can occur at any time and sometimes requires hospital treatment to prevent death.

* A cancer that may occur 20 years after infection. This cancer requires heavy treatment for several months, and 1 out of 3 patients dies from it.

* Condylomas (warts on intimate parts), which can occur at any time. These warts are not dangerous in themselves but can be very annoying. The treatment lasts several months, and warts come back easily.

- The possibility of serious side effects from the vaccine.

- To what extent getting vaccinated also protects other people.

- How many young people have signed up for the vaccine or are being vaccinated elsewhere.

Please note: some of the information comes from other European or English-speaking countries.

Introduction: Instructions (5/5)

In each scenario, you will need to decide whether to register for the immunisation session.

The decision for each scenario will be:

I sign up

I do not sign up

You will then be asked how certain you are of your decision.

* Each scenario is different. Try to make your choice independently of the decisions made in the other scenarios.

* When making your choices, try to take into account all the information presented in the scenarios.

* There are no right or wrong answers. Only your opinion counts.

* You are encouraged to decide without taking into account the opinion that your parents or others may have.

Are you ready?

Supplementary File C –**Modifications made on the attributes and levels**

Characteristics of adolescents testing the preliminary questionnaire via think-aloud
Girl, age 14
Boy, age 13
Girl, age 13
Boy, age 16
Boy, age 10.5

Modifications made on the attributes and levels:

- We removed an attribute on "vaccine effectiveness/controversy" which had two levels because it was judged too complex and not adapted for adolescents. The two levels were "In countries which have been using this vaccine for a while, one sees that the vaccine is very effective against the disease" and "you can read on the internet that one does not know if the vaccine really protects against the disease. It is true, but we know the vaccine is effective against the infection causing the disease".
- We simplified the levels by putting more information in the section introducing the DCE.
 For example, we described the potential diseases in the introduction instead of detailing them in the levels.
- We replaced the Disease level "the vaccine can protect against a disease that leads to complications during pregnancy" by "the vaccine can protect against a disease that gives a high fever and leads to a hospitalisation". We preferred to compare the levels "cancer" and "genital warts" to a usual childhood disease compared to another potential consequence of HPV. Introducing the pregnancy complications was a bit too complicated and could have led participants to think this vaccine is only for females, which we tried to avoid.
- We modified the Safety level "le vaccin est sûr" ("the vaccine is safe") by "Le vaccin ne provoque pas d'effet secondaire grave" ("the vaccine does not provoke serious side effect") because the first version was not well understood by test participants (some thought it meant the vaccine was effective).
- We removed one level of the Safety attribute to reach four levels instead of the original five to simplify the DCE design.
- We modified the Safety level "In countries who vaccinate adolescents for a long time, the risk of developing a serious illness after getting the vaccine has not increased" by "In

countries who vaccinate most adolescents, the risk of a serious side effect which could be due to the vaccine has not increased"

- We modified the "Indirect" level "By getting vaccinated, you can avoid contaminating other persons" by "By getting vaccinated, you can avoid transmitting the infection to other persons." because it was more appropriate wording for this age.
- We replaced the "Coverage" level "Few young people have gotten registered" by "Not enough young people have gotten registered" to insist on the negativity of the statement, which is often used in vaccine communication but goes against social conformism.

Supplementary File D - Average percentage of vaccine acceptance for each scenario; from lowest to highest

						% Theoretical			
					Sexual	vaccine	Number of		
Scenario	Disease	Safety	Indirect Protection	Coverage	Transmission	acceptance	respondents	Total	
13	Febrile Illness	Safety other countries	Individual protection only	Not enough		64.0	224	350	
27	Genital Warts	Safety other countries	Protects others	Not enough		68.1	278	408	
31	Cancer in 20 years	Safety other countries	Individual protection only	Not enough		68.4	327	478	
5	Febrile Illness	Benefit/risk	Protects others	Not enough		70.3	156	222	
38	Genital Warts	Benefit/risk	Protects others	Already one third		72.1	344	477	
7	Cancer in 20 years	Safety other countries	Individual protection only	Already one third		75.7	168	222	
28	Genital Warts	Benefit/risk	Elimination	Other countries 80%		75.7	309	408	
11	Cancer in 20 years	Benefit/risk	Individual protection only	Other countries 80%		76.3	267	350	
36	Febrile Illness	Benefit/risk	Protects others	Other countries 80%		76.9	367	477	
18	Febrile Illness	Safety other countries	Individual protection only	Most students		77.1	270	350	
34	Cancer in 20 years	Benefit/risk	Protects others	Most students		77.4	369	477	
25	Cancer in 20 years	Benefit/risk	Individual protection only	Already one third		77.5	316	408	
37	Genital Warts	No side effect	Individual protection only	Not enough		79.3	378	477	
30	Febrile Illness	No side effect	Individual protection only	Already one third	Yes	80.2	327	408	
4	Febrile Illness	Safety other countries	Elimination	Already one third		80.2	178	222	

22	Cancer in 20 years	Benefit/risk	Elimination	Most students		80.4	328	408
24	Febrile Illness	No side effect	Individual protection only	Already one third		80.9	330	408
15	Genital Warts	Scientific surveillance	Individual protection only	Not enough		81.1	284	350
16	Genital Warts	Safety other countries	Elimination	Most students		81.1	284	350
19	Cancer in 20 years	Safety other countries	Protects others	Other countries 80%		81.4	285	350
2	Cancer in 20 years	Safety other countries	Protects others	Most students		81.5	181	222
21	Febrile Illness	Scientific surveillance	Protects others	Not enough		81.6	333	408
29	Genital Warts	Scientific surveillance	Elimination	Already one third		81.6	333	408
9	Genital Warts	No side effect	Elimination	Not enough		82.0	182	222
20	Genital Warts	Scientific surveillance	Individual protection only	Not enough	Yes	82.3	288	350
35	Genital Warts	Scientific surveillance	Elimination	Other countries 80%		83.2	397	477
32	Cancer in 20 years	Scientific surveillance	Individual protection only	Most students		83.7	400	478
39	Febrile Illness	No side effect	Elimination	Not enough		84.1	402	478
8	Cancer in 20 years	Benefit/risk	Protects others	Other countries 80%		84.2	187	222
40	Genital Warts	Scientific surveillance	Elimination	Other countries 80%	Yes	84.5	404	478
33	Genital Warts	No side effect	Elimination	Most students		84.7	405	478
26	Genital Warts	Scientific surveillance	Individual protection only	Other countries 80%		85.1	347	408
1	Genital Warts	No side effect	Individual protection only	Other countries 80%		85.1	189	222
23	Febrile Illness	Scientific surveillance	Elimination	Most students		85.5	349	408
3	Febrile Illness	Scientific surveillance	Elimination	Already one third		86.0	191	222
6	Cancer in 20 years	Scientific surveillance	Protects others	Already one third		86.0	191	222

14	Febrile Illness	No side effect	Elimination	Other countries 80%		86.9	304	350
10	Cancer in 20 years	Scientific surveillance	Protects others	Already one third	Yes	86.9	193	222
17	Cancer in 20 years	No side effect	Protects others	Already one third		87.1	305	350
12	Febrile Illness	No side effect	Protects others	Most students		87.7	307	350
Total						80.1	11677	14575

The 40 scenarios were divided into four sets of 10 scenarios. Each respondent thus completed 10 scenarios, including one with the additional attribute (sexual transmission).

Response Time	Varied		Uniform		Total		
	%	Count	%	Count	%	Count	
More than 10 minutes	74.4	529	71.62	535	72.98	1064	
Less than 10 minutes	22.93	163	25.84	193	24.42	356	
Missing	2.67	19	2.54	19	2.61	38	
Total	100	711	100	747	100	1458	
<u></u>	0 100						

Supplementary File E – Response Time by Uniform/varied decision

Chi-square test: p-value: 0.433

Supplementary File F – Results of random intercept logit models of vaccination acceptance including interactions between attributes and individual characteristics

	Coefficient	95%CI
Vaccine acceptance		
Attributes		
Disease		
Febrile illness (ref)		
Cancer	-1.21	[-2.33,-0.09]
Warts	0.02	[-0.99,1.03]
Safety		
No side effect (ref)		
Science	0.23	[-0.90,1.35]
Safety other countries	-0.64	[-1.84,0.55]
Benefits	0.94	[-0.28,2.17]
Indirect Protection		
Protect only you (ref)		
Protect others	-0.31	[-0.91,0.30]
Elimination	0.11	[-0.46,0.68]
Coverage		
Not enough (ref)		
Already one third	0.13	[-0.71,0.97]
Most students	0.14	[-0.68,0.96]

Other countries 80%	0.01	[-0.82,0.84]
Attributes * Individual characteristics		
Disease# "It is useful to get vaccinated"		
Cancer#Agree	0.83	[0.06,1.61]
Safety#Age category		
Benefit/risk#14 years old	0.41	[0.04,0.79]
Benefit/risk#15 to 17 years old	0.65	[0.13,1.18]
Safety#Middle school		
Benefit/risk#School 4	-0.89	[-1.58,-0.20]
Safety#" Getting vaccinated can protect others"		
Benefit/risk#Agree	-0.72	[-1.39,-0.04]
Benefit/risk#I don't know	-0.85	[-1.67,-0.03]
Safety#Stated Tdap-IPV vaccine status		
Benefit/risk# I don't know	-1.58*	[-2.69,-0.46]
Benefit/risk#Yes	-1.37	[-2.43,-0.32]
Safety#Stated MenC vaccine status		
Science# I don't know	1.00	[0.22,1.77]
Indirect Protection#" Getting vaccinated can protect others"		
Protects others#Agree	0.71	[0.13,1.28]
Protects others#I don't know	0.71	[0.01,1.41]
Indirect Protection#Stated HPV vaccine status		
Elimination#Yes	0.60	[0.11,1.08]

Coverage#In favour of vaccination

Most students#Agree or strongly agree	0.57*	[0.20,0.95]
Other countries 80%#Agree or strongly agree	0.48	[0.10,0.87]
Coverage# "Vaccination scares me because of the substances in the vaccine"		
Already one third#I don't know	-0.65	[-1.20,-0.10]
Most students#I don't know	-0.72*	[-1.25,-0.19]
Note: variables were included in the final model if they interacted with one or more attributes a	at a p-value<0.10. Only var	iables with interaction at

p-value<0.05 are showcased in this table (*: p-value<0.01).

	Overall RE (N=1458)			Varied decision only RE (n=711)				
	Main I	Effect	Intera	ctions	Main	Effects	Interac	tions
Vaccine acceptance	OR	95%-CI	OR	95%-CI	OR	95%-CI	OR	95%-CI
Disease								
Respiratory disease (reference)	1		1		1		1	
Cancer	1.29	[1.09,1.52]	1.30	[1.09,1.54]	1.25	[1.06,1.48]	1.27	[1.07,1.51]
Warts	0.91	[0.78,1.06]	0.90	[0.77,1.05]	0.88	[0.76,1.02]	0.87	[0.75,1.02]
Safety								
No side effect (reference)	1		1		1		1	
Scientific surveillance	0.86	[0.71,1.04]	0.88	[0.72,1.07]	0.84	[0.70,1.02]	0.85	[0.70,1.03]
Safety other countries	0.30	[0.24,0.36]	0.30	[0.24,0.36]	0.31	[0.25,0.37]	0.30	[0.25,0.37]
Benefit/risk	0.30	[0.24,0.36]	0.29	[0.24,0.36]	0.29	[0.24,0.35]	0.28	[0.23,0.35]
Indirect Protection								
Protect only you (reference)	1		1		1		1	
Protect others	1.30	[1.11,1.52]	1.27	[1.09,1.49]	1.30	[1.11,1.51]	1.28	[1.09,1.49]
Elimination	1.40	[1.18,1.67]	1.40	[1.18,1.66]	1.38	[1.16,1.63]	1.38	[1.16,1.64]
Coverage								
Not enough (reference)	1		1		1		1	
Already one third	1.48	[1.23,1.78]	1.48	[1.23,1.78]	1.54	[1.28,1.84]	1.53	[1.27,1.84]
Most students	1.98	[1.64,2.38]	1.97	[1.63,2.37]	2.04	[1.70,2.45]	2.02	[1.68,2.44]

Supplementary File G – Vaccination acceptance in the "Overall sample" and the "Varied decision only" subsample

Other countries 80%	1.94	[1.61,2.35]	1.92	[1.59,2.33]	2.06	[1.71,2.48]	2.03	[1.68,2.45]
Indirect Protection3(Elimination)* Coverage3(Most students)			1.03	[0.72,1.47]			1.07	[0.76,1.51]
Indirect Protection3(Elimination)* Coverage4(Other countries		0.70	[0 49 1 00]		0.73	[0 52 1 03]		
80%)			0.70	[0.49,1.00]			0.75	[0.52,1.05]

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