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Impact of a school-based and primary care-based multicomponent intervention on HPV vaccination coverage among French adolescents: a cluster randomised controlled trial protocol (the PrevHPV study)

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ABSTRACT

Introduction Vaccination is an effective and safe strategy to prevent Human papillomavirus (HPV) infection and related harms. Despite various efforts by French authorities to improve HPV vaccine coverage (VC) these past few years, VC has remained far lower than in most other high-income countries. To improve it, we have coconstructed with stakeholders a school-based and primary care-based multicomponent intervention, and plan to evaluate its effectiveness, efficiency and implementation through a cluster randomised controlled trial (cRCT).

Methods and analysis This pragmatic cRCT uses an incomplete factorial design to evaluate three components applied alone or in combination: (1) adolescents and parents' education and motivation at school, using eHealth tools and participatory learning; (2) general practitioners' training on HPV using motivational interviewing techniques and provision of a decision aid tool; (3) free-of-charge access to vaccination at school. Eligible municipalities (clusters) are located in one of 14 preselected French school districts and must have only one secondary school which enrols at least 2/3 of inhabitants aged 11–14 years. A randomisation stratified by school district and deprivation index allocated 90 municipalities into 6 groups of 15. The expected overall sample size estimate is 41 940 adolescents aged 11–14 years. The primary endpoint is the HPV VC (≥1 dose) among adolescents aged 11–14 years, at 2 months, at the municipality level (data from routine databases). Secondary endpoints include: HPV VC (≥1 dose at 6 and 12 months; and 2 doses at 2, 6 and 12 months); differences in knowledge, attitudes, behaviours, and intention among adolescents, parents and general practitioners between baseline and 2 months after intervention (self-administered questionnaires); incremental cost-effectiveness ratio. Implementation measures include dose, fidelity, adaptations, reached population and satisfaction (activity reports and self-administered questionnaires).

Ethics and dissemination This protocol was approved by the French Ethics Committee 'CPP Sud-Est VI' on 22 December 2020 (ID-RCB: 2020-A02031-38). No individual consent was required for this type of research; all participants were informed of their rights, in particular not to participate or to oppose the collection of data concerning them. Findings will be widely disseminated (conference presentations, reports, factsheets and academic publications).

Trial registration number NCT04945655.

Strenghts and limitations of this study

- Vaccine coverage is measured using data collected in routine by the national health insurance and vaccination centres, thus avoiding reporting bias.
- Few medicoeconomic analyses of interventions on human papillomavirus (HPV) vaccination uptake are available and mostly concern reminder interventions.
- Assessing impacts on several determinants of vaccination behaviours will help understand how the intervention may promote behavioural change and HPV vaccine uptake.
- Measures of implementation (dose, fidelity, adaptations, reached population and satisfaction) will help stakeholders decide how the intervention may be replicated or generalised at a national level.
- Due to feasibility constraints, large French municipalities are not included in the study, and a possible selection bias in the future results cannot be excluded.

INTRODUCTION

Human papillomavirus (HPV) infection is the most common viral infection of the reproductive tract, and a major public health issue.[1 2]

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More than 80% of sexually active men and women will acquire HPV by age 45,[3] often shortly after the onset of sexual activity.[1] Most HPV infections (70%–90%) are asymptomatic and resolve spontaneously.[2] However, persistent infections can cause anogenital warts, precancerous lesions of the cervix, vagina, vulva, anus, penis and head and neck, which, if untreated, may sometimes progress to cancers.[2] Worldwide, HPV contributed to about 690 000 new cases of cancers in 2018 (ie, 4% of all cancers; women: 620,000; men: 70,000).[4] Cervical cancer is by far the most common HPV-related cancer,[2] with 7 out of 10 cases caused by two high-risk HPV types (16 and 18).[5] It is the fourth most frequent cancer in women worldwide, accounting for 604 127 new cases and 341 831 deaths in 2020 (respectively, 3379 and 1452 in France).[6 7]

Vaccination is the most effective primary prevention strategy against HPV infection.[2 7] It protects against HPV infections, anogenital warts and high-grade precancerous cervical lesions (ie, cervical intraepithelial neoplasia (CIN) 2+ and CIN3+).[8–11] After 5–8 years of vaccination, data from 14 countries showed a significant decrease in the prevalence of HPV 16 and 18 infections (−83% among girls aged 13–19 years), anogenital warts diagnoses (−67% and −48% among girls and boys aged 15–19 years, respectively) and CIN2+ (−51% among girls aged 15–19 years), with a greater decrease in countries with both a wider range of targeted age groups and high vaccine coverage (VC).[10] More recently, HPV vaccination has been associated with a reduced risk of invasive cervical cancer among Swedish girls/women aged 10–30 years.[12] HPV vaccines have an 'excellent safety profile' according to the WHO,[2] with adverse events generally being non-serious and of short duration. Moreover, a study on postlicensure safety surveillance did not find any association between HPV vaccination and some conditions (eg, autoimmune diseases) that have occurred postvaccination.[2]

Since 2006, most high-income countries have introduced HPV vaccination in their vaccination schedules for adolescents (for girls only or girls and boys, depending on the country).[13 14] In France, HPV vaccination was initially recommended for girls when it was introduced in 2007; in 2021, it was included in the vaccine schedule for all adolescents aged 11–14 years.[15] The currently recommended vaccine is the latest nonavalent one (against 6, 11, 16, 18, 31, 33, 45, 52, 58 types) with two injections 6 months apart.[15] A catch-up with three injections is possible up to age 19 years. HPV VC varies significantly across high-income countries, from a few percentage points (eg, in Poland, Bulgaria) to 90% (eg, in Norway and Iceland).[13 14] Almost 15 years after HPV vaccine introduction in France and despite various efforts by health authorities to improve HPV vaccine uptake,[16 17] complete HPV VC remains lower than in most other high-income and European countries,[13 14] having been estimated at 23.7% among 16-year girls in 2018.[18] In this context, the French Institute for Public Health Research (IReSP) and the theme-based Multi-Organisation Institutes for Cancer and for Public Health (ITMO Cancer and ITMO Public Health) launched in 2018 a national research programme to improve HPV VC among French adolescents. This research programme in epidemiology and social and human sciences is conducted by a consortium of eight French teams (The PrevHPV Consortium—see list in online supplemental table 1) and funded as part of the National Cancer Plan 2014–2019. This programme, called the PrevHPV programme, includes the following three phases.

The first 'diagnostic' phase (October 2019–March 2021) aimed at exploring knowledge, beliefs, behaviours, practices, barriers, motivations and preferences towards HPV vaccination among four population groups: girls and boys from secondary schools (aged 11–14 years); their parents; staff from schools (eg, teachers, nurses); and general practitioners (GPs). This phase included several quantitative and qualitative surveys, according to a mixed method approach, and manuscripts reporting results are being written (for preliminary results see[19 20]).

The second 'coconstruction' phase (October 2019–June 2021) aimed at designing the multicomponent intervention to improve HPV VC. Three components were identified: adolescents' and parents' education and motivation at school (component 1); GPs' training (component 2); and access to vaccination at school (component 3) (see 'The three components of the intervention' section).

The third 'experimental' phase, yet to be conducted (November 2021–May 2022), aims at evaluating the effectiveness, efficiency and implementation of the intervention in France, taking into account its multicomponent structure, through an incomplete factorial design and using cluster randomisation (called the PrevHPV study).

The present manuscript describes the protocol of this cluster randomised trial (cRCT) using the 'Standard Protocol Items: Recommendations for Interventional Trials' (SPIRIT) statement as a guide[21] (see completed SPIRIT checklist in online supplemental table 2).

METHODS AND ANALYSIS

Study organisation

The French National Institute for Health and Medical Research (Inserm) is the sponsor of the PrevHPV study. A scientific and operational committee (called PrevHPV Study Group) is in charge of supervising all scientific aspects and organisational issues occurring during the PrevHPV programme and meets monthly to elaborate, perform and follow the research. This committee comprises the scientific leaders of each of the eight teams involved in the consortium and their staff, and a representative from IReSP and from Inserm.

A steering committee is in charge of supervising the progress of all aspects of the PrevHPV programme, and meets once a year. It comprises the scientific leaders of the eight teams, as well as representatives of the following national institutions: Inserm, IReSP, ITMO Cancer AVIESAN, ITMO Public Health AVIESAN, INCa (French National Cancer Institute), Santé publique France

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(French Public Health Agency), Ministry of Health, Ministry of National Education, and the Ile-de-France Regional Health Agency.

Patient and public involvement

The three components of the intervention (see 'The three components of the intervention' section) are developed using results from our diagnostic phase on target populations' needs. The public (adolescents, parents, GPs and school staff) is involved in the activities/tools development based on a participatory approach in a coconstruction process. As part of the component 1, educational group sessions on HPV infections and vaccination are delivered to pupils by regular school staff. The public is not involved in the design and the recruitment stage of the study.

Study objectives and endpoints

The primary objective of the PrevHPV study is to evaluate the effectiveness of a multicomponent intervention (components being applied in combination or alone) on the HPV VC among adolescents (girls and boys) aged 11–14 years at the municipality (cluster) level. The corresponding endpoint is the HPV VC (≥1 dose) 2 months after the end of intervention's implementation (ie, the prevalence of adolescents aged 11–14 years who have received at least one dose of HPV vaccine). HPV VC (≥1 dose) at 6 and 12 months, and HPV VC (two

Table 1 Endpoints of the PrevHPV study

Dimension/measure	Target population	Data sources	Time frame
Vaccine coverage (main objective)			
≥1 dose	Adolescents 11–14 years	Health insurance (SNDS), vaccination centres	M2, M6, M12
2 doses	Adolescents 11–14 years	Health insurance (SNDS), vaccination centres	M2, M6, M12
Knowledge, beliefs, behaviours, practices, intention towards HPV vaccination (secondary objective 1)			
Items of the KABP-6C questionnaire	Adolescents, parents and GPs	Self-administered online questionnaires	Before intervention, M2
Efficiency (secondary objective 2)			
Incremental cost-effectiveness ratio	Adolescents 11–14 years	Costs of the intervention, Health insurance (SNDS), vaccination centres	M2, M6, M12
Annual cost and health gains of generalising the component(s) at the national level*	Adolescents 11–14 years (whole country)	Costs of the intervention, Health insurance (SNDS), vaccination centres	/
Intervention components' implementation (secondary objective 3)			
Intervention components' dose and fidelity: activities performed according to the frame of reference for each component, use of tools developed for each component (assessment of the gap between activities/tools planned and activities/ tools really performed/used)	/	Regular activity reports collected on a standardised form during components' implementation	
Reached populations: percentage of target individuals who benefit from (or participate in) activities of each component (assessment of the acceptability of each component)	Adolescents, parents, school staff and GPs	Regular activity reports collected on a standardised form during components' implementation	
Intervention components' adaptation: components modified to adapt them to the local context/environment of each school/municipality	/	Regular activity reports collected on a standardised form during components' implementation	
Satisfaction of target populations regarding each activity/component and identification of barriers and levers to components' implementation	Adolescents, parents, schools and vaccination centres' staff and GPs	Self-administered (paper or online) questionnaires collected at the end of the components' implementation	

*Costs associated with generalising effective component(s) at 1 and 5 years will be compared with the corresponding health gains in terms of size of the vaccinated population (1 and 2 doses).
GPs, general practitioners; HPV, human papillomavirus; KABP-6C, Knowledge, attitude, behaviours, practices and six psychological determinants of vaccination intention (Confidence, Complacency, Constraints, Calculation, Collective responsibility and social Conformism); SNDS, Système National des Données de Santé.

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doses) at 2, 6 and 12 months are secondary endpoints (table 1).

Secondary objectives are to evaluate:

(1) The impact of the multicomponent intervention (components being applied in combination or alone) in target populations (adolescents, parents and GPs) on knowledge, beliefs, behaviours and practices towards HPV vaccination, intention to initiate HPV vaccination and psychological determinants of vaccination intention; (2) the efficiency (cost-effectiveness) and the budget impact of the components and components' combinations that are effective and (3) the implementation of the components of the intervention, and barriers and levers of implementation at both individual and community level.

Endpoints corresponding to secondary objectives are described in table 1.

The three components of the intervention

The intervention comprises three components implemented at a territorial level (a municipality). Components target (1) adolescents aged 11–14 years, who are the target population for HPV vaccination in France, and their parents, who decide whether to vaccinate their child; (2) GPs, who prescribe most HPV vaccines in France,[22] and have a fundamental role in patients' decision-making process towards vaccination.[23]

Evidence from the literature shows that adolescents' and parents' lack of knowledge on HPV infection and vaccine effectiveness and safety are strong barriers to HPV vaccination.[23 24] They may also face financial and organisational barriers to HPV vaccination as usual pathway to access vaccination in France is rather complex.[14] In general, adolescents and their parents have to take an appointment with a physician to get the vaccine prescription, then go to a community pharmacy to obtain the vaccine, and finally take another appointment with their physician for its administration. Occasionally, individuals may also benefit from vaccination going to hospital vaccination centres, but their geographical accessibility can be difficult. Besides, HPV vaccine is only partially reimbursed by the French national Health Insurance, and some patients may be charged out-of-pocket costs.[14]

As for GPs, they face difficulties in informing patients on vaccination and need to acquire educational techniques to improve their communication with vaccine hesitant patients.[25]

Component 1 ('Adolescents' and parents' education and motivation at school') first includes a webconference on HPV infection and vaccination for parents. Second, adolescents participate during school hours to two educational group sessions on HPV infections and vaccination, using eHealth tools (videos, serious video game) and participatory learning.

Component 2 ('GPs' training') consists of an individual e-learning training session including: (1) an updated information on HPV infection and vaccination; (2) an introduction to the use of motivational interviewing techniques in the field of vaccination and (3) a presentation of the decision aid tool developed as part of the intervention. This tool aims at helping hesitant individuals to take a decision about HPV vaccination and will be provided to GPs who have attended to the training.

Component 3 ('HPV vaccination at school') consists of a vaccination day on school premises where health professionals from local vaccination centres initiate HPV vaccination free of charge and without any medical prescription for all eligible adolescents (see 'Target populations' section).

Study design and setting

The PrevHPV study is a pragmatic cRCT,[26] using an incomplete factorial design. The unit of randomisation (cluster) is the municipality. The factorial design allows to evaluate the multicomponent intervention taking into account that each component could be applied alone or in combination with other(s) component(s); however, it is incomplete because the PrevHPV Study Group considers that access to vaccination at school (component 3) should not be implemented without prior adolescents' and parents' education and motivation (component 1). Eventually, 6 groups are compared in this study (figure 1), and we randomly allocated 15 municipalities to each group.

Two components (1 and 3) are set in secondary schools, whereas component 2 targets GPs practising in private practice in the participating municipalities.

The intervention will be implemented from December 2021 to March 2022 (table 2).

Eligibility and allocation of municipalities

Fourteen of the 25 school districts spread over the French territory were first selected by the PrevHPV Study Group together with representatives of the Ministry of National Education to ensure a diversity of geographical, demographic and socioeconomic profiles.

Municipalities were eligible if: (1) they were located in one of the selected school districts; (2) there was only one secondary school (for pupils aged 11–14 years) in the municipality; and (3) at least 2/3 of inhabitants aged 11–14 years attended the municipality's secondary school. Out of 1205 eligible municipalities, we randomly sampled 351 (see details in online supplemental text 1) and contacted the head of the secondary school located in each municipality by mail and by phone to ask him/her to participate in the study. The first 90 municipalities for which the secondary school agreed to participate were included in the study.

A block randomisation (block size=6) stratified by school district and French deprivation index (see definition in online supplemental table 3) then allocated the 90 municipalities into six groups (group 1–6) of 15 municipalities (figure 1). This randomisation was performed by a senior researcher of the PrevHPV Study Group not involved in the selection process of the municipalities.

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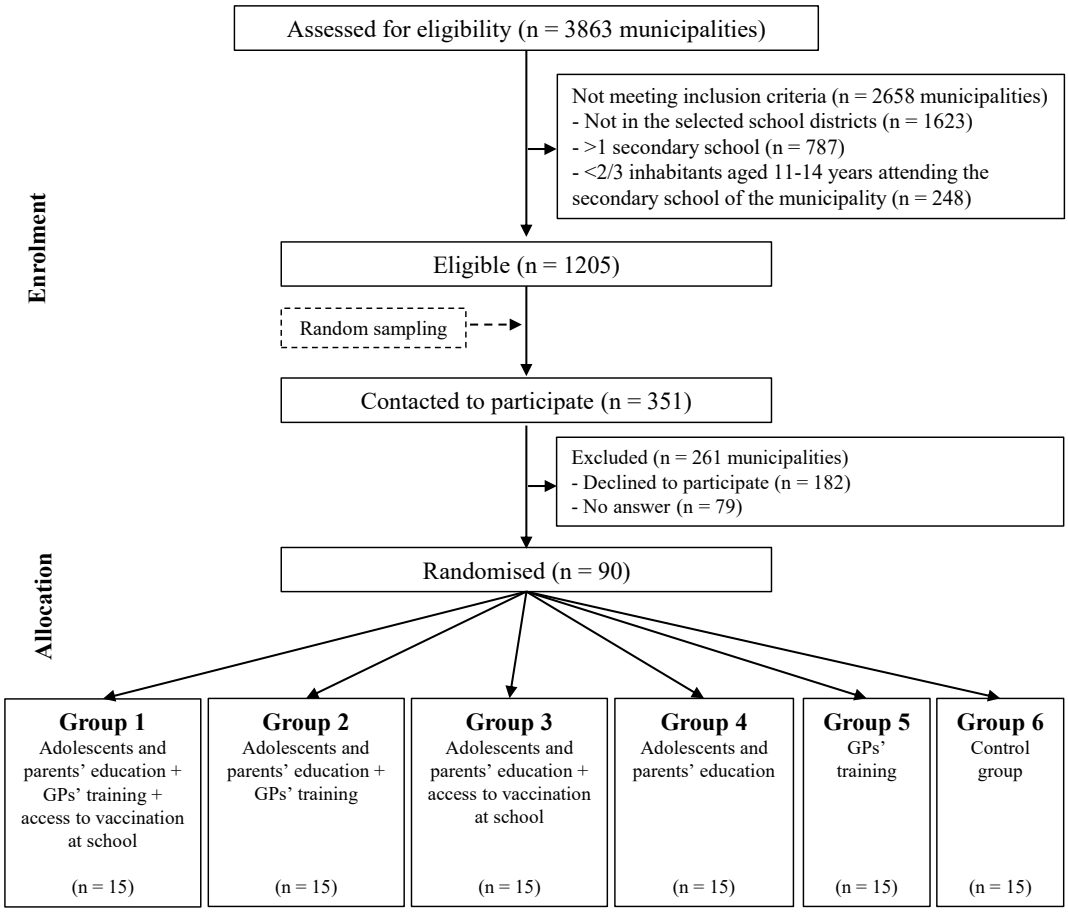

Figure 1 PrevHPV study flow chart of expected number of participating municipalities. GPs, general practitioners; HPV, human papillomavirus.

Target populations

For adolescents' and parents' education and motivation at school (component 1), the target populations of the intervention are: adolescents attending secondary school in the 60 municipalities from groups 1 to 4 (figure 1) and their parents; for GPs' training (component 2): GPs' practising in the 45 municipalities from groups 1, 2 and 5; for access to vaccination at school (component 3): adolescents attending secondary schools of the 30 municipalities from groups 1 and 3, never vaccinated against HPV, ≥11 years old, with no contraindication to vaccination, and whose parents have given their written consent to vaccinate their child. Populations included in the statistical analyses are slightly different (see details in online supplemental table 3).

Data collection

HPV VC (at least 1 dose and 2 doses) at 2, 6 and 12 months after components' implementation in ad hoc groups will be estimated using data from two sources. The first source is the French health insurance database (Système National des Données de Santé, SNDS). Prospectively recorded for all beneficiaries of healthcare in France, the SNDS covers almost the entire French population (67 million inhabitants).[27] This database contains individualised and anonymous data on all medical expenditure reimbursements, and most HPV vaccines in France are delivered in community pharmacies and recorded in the SNDS. The second source of data are registries data from vaccination centres which serve participating municipalities (including the number of vaccines delivered as part of component 3), as vaccines administrated by vaccination centres are not recorded in the SNDS. Some characteristics (eg, age, gender, municipality of residence) of each individual who benefits from a medication reimbursement by the French health insurance or a vaccine administration in a vaccination centre are also recorded, allowing us to estimate an HPV VC prevalence per municipality. Total number of inhabitants aged 11–14 years (denominator) will come from the SNDS. Data necessary to calculate HPV VC before the intervention implementation will also be collected to adjust for baseline VC rate by group in the analyses.

Self-administered online questionnaires will be distributed among adolescents attending participating schools, their parents, and GPs located in included municipalities to collect data for the first secondary objective (tables 1 and 2), before and after the components' implementation in ad hoc groups. Changes in knowledge, beliefs, behaviours and practices, intention to initiate HPV vaccination as well as psychological determinants of vaccination

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Table 2 The PrevHPV study schedule of enrolment, intervention's components and endpoints measurements

GPs, general practitioners; HPV, human papillomavirus; KABP-6C, Knowledge, attitude, behaviours, practices and six psychological determinants of vaccination intention (Confidence, Complacency, Constraints, Calculation, Collective responsibility and social Conformism); VC, vaccine coverage.

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intention based on the '6C' model (Confidence, Complacency, Constraints, Calculation, Collective responsibility and social Conformism)[28–30] will be assessed using online KABP-6C questionnaires for adolescents (in-class participation) and parents, linking preassessments and postassessments by anonymous identifiers. Basic demographic and socioeconomic characteristics will also be collected (eg, gender, age, parents' educational level, and, for GPs, years of experience, type of practice) for each target population.

Indicators have been defined to assess the resources (human, material, financial) consumed for the conception and implementation of each component,[31] tools used and activities realised, and populations reached by different activities. Data to calculate these indicators will be regularly collected during the study period by the professionals involved (eg, PrevHPV staff, schools' staff, GPs, vaccination centres' staff) through activity reports questionnaires (tables 1 and 2).

Satisfaction of target populations and involved professionals regarding each activity/tool, as well as barriers identified and levers we may use to implement components will be assessed using self-administered paper or online questionnaires filled out at the end of the implementation phase in groups 1–5.

The scientific leaders of the PrevHPV consortium will have access to the final study dataset.

Sample size

For the sample size calculation, we have retained the hypothesis that all adolescents living in a municipality attend the secondary school of this municipality, and used the average number of pupils per secondary school (466, with a coefficient of variation about 0.5, according to data from the Ministry of National Education) as the mean cluster size. The HPV VC (≥1 dose) among all French adolescents is estimated to be at around 8% specifically in the age group of 11–14 years for the two genders,[18] knowing that it is close to 0% in boys, for whom it was not included in vaccine schedule until 2021.

Considering an intraclass correlation of 0.05, a sample of 15 municipalities per group would be sufficient to detect an increase of 10 percentage points in the VC between two groups, with a 90% power and a 5% α risk.

We, therefore, included 90 municipalities, that is, 15 per group, in the PrevHPV study. This corresponds to an expected sample of 41 940 adolescents aged 11–14 years.

Statistical analyses

The PrevHPV Study Group defined a statistical analyses plan. Briefly, it includes the following procedures:

1. A description of the main sociodemographic characteristics (of GPs, of adolescents/parents at the secondary school and municipality levels) overall and per group.
2. A calculation of the HPV VC prevalence (≥1 dose and 2 doses) among adolescents aged 11–14 years at baseline, 2, 6 and 12 months, in each municipality and in each of the six groups.
3. A comparison of HPV VC at different times between groups using a linear model including fixed effects (one per component and interactions between components), adjusted for baseline VC. Units of analysis will be municipalities. Subgroup analyses according the adolescents' gender and the municipalities' deprivation index will be performed using interaction terms.

For the first secondary objective, scores of knowledge, beliefs, practices and psychological determinants of vaccination intention will be calculated per municipality and per group before and after the intervention, along with the differences between the two measures. The percentage of target individuals (adolescents, parents, GPs) who change positively towards intention/vaccination (ie, unvaccinated people who had no intention to get vaccinated at baseline but who either intend to get vaccinated or initiate the vaccination after the intervention) by municipalities and by groups will also be estimated. The impact of each component and their combination on these variables will then be assessed using a multilevel model that takes into account the hierarchical structure of the data (individuals nested in schools), adjusted for relevant characteristics identified in step (1). The cost-effectiveness analyses will be performed according the French Health High Authority guidelines for economic evaluations[32] from an all-payers perspective, with a time horizon of 2 months after the end of the intervention, with secondary analyses at 6 and 12 months. Only direct costs will be considered (costs of component(s), vaccines and medical consultations). The effectiveness criterion will be the difference in HPV VC prevalence (≥1 dose) between baseline and 2 months after intervention. An incremental cost-effectiveness ratio will then be calculated to estimate the incremental cost per increase of 10 percentage points in the VC prevalence for each component as compared with controls and for the component(s) combined to build an efficiency frontier. Deterministic and probabilistic sensitivity analyses will evaluate the robustness of the results. A budgetary impact analysis will then assess the costs associated with generalising effective component(s) at 1 and 5 years, which will be compared with the corresponding health gains in terms of size of the vaccinated population (1 and 2 doses). The time horizon will be too short to assess the impact on cancers and deaths prevented.

All analyses will be performed in intention to treat, using SAS V.9.4 or a future version (SAS Institute), R or STATA V.15.1 or a future version.

Ethics and dissemination

This study was granted approval by the French Ethics Committee 'Comité de Protection des Personnes—CPP Sud-Est VI' on 22 December 2020 (ID-RCB: 2020-A02031-38). No individual consent was required for this type of research; all participants (adolescents, parents of adolescents and GPs) were informed of their rights, in particular not to participate or to oppose the collection of

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data concerning them (see information sheets in online supplemental text 2).

Findings of this study will be widely disseminated through conference presentations, reports, factsheets and academic publications and generalisation will be further discussed.

DISCUSSION

The PrevHPV study is a pragmatic cluster randomised controlled study included in a major national research programme supported by the French health authorities. Conducted by a multidisciplinary consortium, it aims at evaluating the effectiveness, efficiency and implementation of a multicomponent school-based and primary care-based intervention on HPV vaccine uptake among French adolescents, taking into account the constraints of the environment in which intervention is implemented. This study has several strengths. First, it measures main endpoints (VC) using data collected in routine by the national health insurance and vaccination centres. These data are more reliable than self-reported ones and avoid reporting bias.[33] Second, we designed the intervention using results from our diagnostic phase on target populations' needs, and used a participatory approach in a co-construction process involving adolescents, parents and GPs in the activities/tools development.[34] This approach is recommended to enhance the feasibility, effectiveness and acceptability of health interventions.[35] We should also acknowledge some limits. We assess VC at the municipality level which is the smallest geographical scale available in routine SNDS databases. As a result, inclusion of municipalities with more than one secondary school would have required that all schools in that municipality accept to participate. To ensure the study feasibility, we limited the study to municipalities with only one secondary school, and thus excluded all large French municipalities. Thus we cannot exclude a possible selection bias in our future results, but a French study using the SNDS database found that HPV vaccine uptake did not vary significantly according to the number of inhabitants in a municipality after adjustment for individual and other area level characteristics (eg, deprivation index, density of gynaecologists).[36]

The factorial design of this study will provide results on the effectiveness of each of the three components, applied alone or in combination with the other(s). It will add to the small number of studies that compared the effectiveness of different kind of strategies to promote vaccination, as categorised by the Community Guide[23 37 38]: interventions to increase community demand for vaccination; provider/system care-based interventions; interventions to enhance access to vaccination services. Our study will provide a wide range of other results, including efficiency (cost-effectiveness), when very few economic evaluations of interventions about HPV vaccination are available, and mostly concern reminder/recall interventions.[38] Data on implementation (dose, fidelity, adaptations, reach and satisfaction of target populations) are also critical information for stakeholders to help them decide how the intervention may be replicated[39] and possibly generalised at a national level.

To gain understanding of how the intervention may promote behaviour change and HPV vaccine uptake among adolescents, we will assess the impact of the intervention on several determinants of vaccination behaviours and intention, among adolescents, theirs parents and GPs. Exploring causal pathways between intervention activities/tools and outcomes may help understand how these effects may be replicated by similar future intervention.[39]

Finally, the design of the PrevHPV study allows participation of municipalities with different deprivation levels and a balanced allocation between the study's groups. We plan to assess in exploratory objectives whether and how results vary according to deprivation levels and the impact of the intervention on social inequalities in HPV vaccine uptake. Thus, this study will contribute to pay greater attention to equity in implementation science.[40]

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Contributors MM, BG, KC and NT developed the study protocol with input from AB, SB, AG-B, AG, SG, A-SLD-B and JM; ABG led the development of the adolescents

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and parents' education and motivation component; SG led the development of the general practitioners' training component; A-SLD-B led the development of access to vaccination at school component; SB facilitated the partnership between the teams of the consortium, and with the steering committee; AB and NT drafted the first version of the manuscript and all authors provided comments and feedback for improvement the manuscript. All authors approved the final version of the manuscript and are responsible for their contributions.

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Supplementary File

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Supplemental table 1 Teams conducting the PrevHPV programme (The PrevHPV Consortium)

Team n°	Contact/scientific leader	Field of expertise
1	EA 4360 APEMAC - Université de Lorraine 9 av. de la Forêt de Haye - BP 20199 - 54505 VANDOEUVRE LES NANCY Cedex Scientific leader, principal investigator: Pr THILLY Nathalie (email: n.thilly@chru-nancy.fr)	Epidemiology and Public health
2	Département de Médecine Générale - Université Paris - 24 rue du Faubourg Saint-Jacques -75679 PARIS Cedex 14 Scientific leader: Pr GILBERG Serge (email: sergegilberg@gmail.com)	Primary Care
3	Laboratoire Interuniversitaire de Psychologie - UFR Sciences de l'Homme et de la Société - Université Grenoble Alpes BP 47 - 38040 GRENOBLE Cedex 9 Scientific leader: Dr GAUCHET Aurélie (email: aurelie.gauchet@univ-grenoble-alpes.fr)	Health Psychology
4	CRCDC Pays de la Loire 5 rue des Basses Fouassières - 49000 ANGERS Scientific leader: Dr LE DUC-BANASZUK Anne-Sophie (email: as.banaszuk@depistagecancers.fr)	Public Health, Cancer prevention
5	Campus Santé Innovations - Faculté de Médecine Jacques Lisfranc 10 rue de la Marandière - 42270 SAINT-PRIEST-EN-JAREZ Scientific leader: Dr GAGNEUX-BRUNON Amandine (email: amandine.gagneux-brunon@chu-st-etienne.fr)	Infection Diseases
6	INSERM UMR 1123 ECEVE, Université de Paris,75010 PARIS Scientific leader: Pr CHEVREUL Karine (email: karine.chevreul@inserm.fr)	Health Economics
7	Institut Pasteur - 25 rue du Dr Roux - 75724 Paris cedex 15 Scientific leader: Dr MUELLER Judith (email: judith.mueller@ehesp.fr)	Epidemiology and Public health
8	CHRU de Tours - Centre d'investigation Clinique Bretonneau - 37044 Tours cedex 9 Scientific leader: Pr GIRAUDEAU Bruno (email: bruno.giraudeau@univ-tours.fr)	Biostatistics

Supplemental table 2 SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed in section
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	Title page
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	Title page
	2b	All items from the World Health Organization Trial Registration Data Set	See Clinicaltrials.gov, NCT04945655
Protocol version	3	Date and version identifier	Title page
Funding	4	Sources and types of financial, material, and other support	Funding section
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	Title page
	5b	Name and contact information for the trial sponsor	See Clinicaltrials.gov, NCT04945655
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	Funding section
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	Study organisation

Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	Introduction
	6b	Explanation for choice of comparators	Introduction
Objectives	7	Specific objectives or hypotheses	Study objectives and endpoints
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	Study design and setting
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	Study design and setting
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	Eligibility and allocation of municipalities & Target populations
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	The three components of the intervention & Table 2
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	NA (public health research)
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	NA (public health research)

	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	NA (public health research)
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	Study objectives and endpoints & Table 1
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	Table 2
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	Sample size
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	Data collection
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	Eligibility and allocation of municipalities
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	Eligibility and allocation of municipalities
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	Eligibility and allocation of municipalities
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	NA

	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	NA
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	Data collection
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	NA
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	Details on the study's e-case report form and data management available on request.
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	Statistical analyses
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	Statistical analyses
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	Primary endpoints: no missing data (health insurance database)

Methods: Monitoring

Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	Not required (in accordance with the French law regarding this type of research, and with the ethics committee's agreement)
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	NA
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	NA (organisational intervention)
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	NA

Ethics and dissemination

Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	Ethics and dissemination
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	Ethics and dissemination
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	See Item 32
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	NA

Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	Data collection
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	Competing interests
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	Data collection
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	NA
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	Ethics and dissemination
	31b	Authorship eligibility guidelines and any intended use of professional writers	NA
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	NA
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	No individual consent required for this type of research (information sheets available in Supplemental text 2)
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	NA

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license. NA: not applicable.

Supplemental table 3 Populations included in the statistical analyses

Endpoints	**Population included in analyses**	**Groups**
Vaccine coverage	Inhabitants of the municipality aged 11-14 years	1-6
KABP-6C	Adolescents attending the secondary school of the municipality	1-6
	Parents of adolescents attending the secondary school of the municipality	1-6
	GPs practicing in the municipality	1, 3, 5
Satisfaction regarding the intervention(s)/tool(s)	Adolescents attending the secondary school of the municipality	1-4
	Staff of the secondary school of the municipality	1-4
	GPs practicing in the municipality	1, 3, 5

GPs: general practitioners; KABP-6C: Knowledge, attitude, behaviours, practices and six psychological determinants of vaccination intention (Confidence, Complacency, Constraints, Calculation, Collective responsibility and social Conformism).

Supplemental text 1 Random sampling design

As part of the recruitment procedure, 351 municipalities were randomly selected from 1,205 eligible ones. Sampling was stratified for the school district and the French deprivation index [1] of the municipality. Due to feasibility constraints, municipalities located in schools districts/regions of the PrevHPV consortium were oversampled, using the following sampling ratios:

(i) Municipalities of school districts where one team of the consortium is located: 1/2;

(ii) Municipalities of school districts where no team of the consortium is located, but belonging to a region where a team is located: 1/5;

(iii) Municipalities of other selected school districts: 1/8.

The French deprivation index was dichotomised according to the median in the school district. This index is available by municipality in the French health insurance database (Système National des Données de Santé, SNDS). It is defined as the first component of a principal component analysis (PCA) of four variables coming from census data: the median household income, the percentage of high school graduates in the population aged 15 years and older, the percentage blue-collar workers in the active population, and the unemployment rate.

Reference

1. Rey G, Jougla E, Fouillet A, Hémon D. Ecological association between a deprivation index and mortality in France over the period 1997 – 2001: variations with spatial scale, degree of urbanicity, age, gender and cause of death. BMC Public Health. 2009;9:33.

Supplemental text 2 Information sheets (translated in English by the authors for the purpose of the publication)

Bocquier A, *et al. BMJ Open* 2022; 12:e057943. doi: 10.1136/bmjopen-2021-057943

A) Parents' information sheet (for groups 1 and 3)

PARENTS' INFORMATION SHEET

Version N°**4.0 07/10/2021**

N° Inserm	N°IDRCB	N° CPP	N°CNIL
C20-76	2020-A02031-38	AU 1655	921334

Dear Madam, Sir,

Your child's secondary school participates in the PrevHPV project ("Evaluation of a multicomponent intervention aiming at improving the acceptability of Human Papillomavirus (HPV) vaccination in France") coordinated by Pr Nathalie THILLY, investigator-coordinator[1] of this project.

The PrevHPV project is conducted by 8 research teams with expertise in Epidemiology, Social and Human Sciences and Primary Care. It is a multicentre study, i.e., conducted in several secondary schools in France.

This project is also supported by the Direction Générale de l'Enseignement Scolaire (DGESCO).

The purpose of this document is to give you written information to help you decide whether or not you and your child will participate in this project. You are free to participate or not. During the course of the project, if you need additional information, do not hesitate to ask questions to the head of your child's school or to the project referent (whose name appears on the project label stuck in your child's home-school liaison booklet). Persons under judicial protection are not eligible to participate in this study.

The Inserm, Institut National de la Santé et de la Recherche Médicale, is the sponsor[2] of this project (*Inserm - Pôle Clinique – Biopark, Bâtiment A 8 rue de la Croix Jarry 75013 Paris*).

1. CONTEXT, OBJECTIVES AND JUSTIFICATION

HPV infection is the most common viral infection of the reproductive tract worldwide.

It is associated with an increased risk of some cancers (cervix, vagina, vulva, penis, anus and oropharynx) among women and men.

Vaccination against HPV has been available for more than 10 years. It is effective against 90% of the HPV infections responsible for cancers and also protects against anogenital warts (also called condylomas).

Until 2019, vaccination was mainly recommended for young girls, but despite many reassuring data on the effectiveness and safety of the vaccine, less than 30% of girls aged 11 to 14 years are vaccinated in France.

In order to better fight this virus, as of December 16, 2019, it was decided to recommend the vaccine for boys aged 11 to 14 years too.

The aim of the PrevHPV project is to propose the implementation of different actions within secondary schools and to observe whether these actions allow increasing the number of vaccinated adolescents (girls and boys aged 11-14).

[1] The investigator is the person responsible for the conduct of the research at a trial site. If the research involves several investigators, one investigator-coordinator is appointed among them.

[2] The sponsor is an individual, company, institution, or organization which takes responsibility for the initiation, management, and/or financing of a trial.

2. DESCRIPTION OF THE PROJECT

As part of the PrevHPV project, the intervention includes different actions that will be carried out within your child's school:

- **Some questionnaires will be completed online**, twice, by you and your child (if he/she is in 9th or 10th grade). The first questionnaire will be sent to you shortly and the second questionnaire will be completed in a few months. This step will take 15 minutes per questionnaire.

  These questionnaires aim at assessing your and your child's knowledge and perceptions about HPV infection and vaccination. Your child will complete the questionnaires during class hours and you will soon receive a web link to fill out the questionnaires yourself.

- Then, your child (if he/she is in 9th or 10th grade), will participate in educational sessions on HPV infections and vaccination as part of the school curriculum (sessions entitled "Education, Motivation and Mobilisation").

  During these sessions, specific tools developed as part of this project will be used (serious game, videos...). At the same time, **information meetings will be offered to you, the parents, whatever your child's grade (from 7th to 10th).** During these meetings, information on HPV infections and vaccination will be provided and you will be able to ask questions on this subject.

Then, if your child has not yet been vaccinated, he/she will be able to get vaccinated against HPV directly at school, subject to your agreement, during a day dedicated to vaccination. During this day, a physician and a nurse, working in a vaccination centre and used to vaccinate, will be present to vaccinate the teenagers whose parents (holders of the parental authority) have given their written consent. The project referent of your child's school will give you additional information on this intervention conducted by the vaccination centre soon. You are free to accept or refuse your child's vaccination. And, if you wish to refer to your general practitioner (or any other health professional of your choice) for this vaccination, this remains also possible.

For all participating municipalities, the number of vaccinated and unvaccinated adolescents aged 11-14 years will be collected using data from the Système National des Données de Santé (anonymous data on vaccines delivered in community pharmacies) and from vaccination and family planning centres (also anonymous data). These data will be collected before the intervention and then 2 months, 6 months and 12 months after the end of the intervention. These data will allow us to measure the impact of our project on the percentage of adolescents vaccinated against HPV.

Duration of your participation: 6 months
Total duration of the project: 6 years

3. EXPECTED BENEFITS, CONSTRAINTS, RISKS AND SPECIFIC PROJECT PROCEDURES

There is no risk associated with participating in this project.

Your and your child's participation is voluntary. You and your child are free not to answer the questionnaires. And if you agree to participate, you can stop your participation at any time for you and/or your child, without incurring any liability or prejudice as a result. Finally, if you do not want your child to answer the questionnaires during school hours, you just have to inform the head of the school or the project referent, whose name appears on the project label stuck in your child's home-school liaison booklet.

The results of this project will allow a better understanding of vaccination preferences from a scientific research perspective. These data can then help increase vaccination coverage in France and decrease the number of HPV-related infections in the population.

For more information or to discuss about vaccination, you can contact your general practitioner or visit the website https://vaccination-info-service.fr/

4. CONFIDENTIALITY AND PROCESSING OF YOUR AND YOUR CHILD'S PERSONAL DATA

As part of this project, the processing of your personal data and those of your child (in particular your age, sex, school municipality) will be performed to enable the analysis of the research's results. The execution of the public interest mission entrusted to Inserm justifies the processing of your personal data and that of your child for scientific research purposes. The collected data will not be directly identifying. These data will be identified by a non-identifying confidential number (participant code) which you will receive and be the only one able to enter. There will be no correspondence between this participant code and your child's identity.

How long your and your child's data will be retained and archived as part of this project:

The data collected through the questionnaires will be analysed by the PrevHPV teams under the responsibility of the investigator-coordinator.

Your and your child's data will be kept in the secure information systems of the PrevHPV consortium's data controller for a maximum of 7 years (duration of the project + 1 year necessary for the writing of the final report). Then, the data will be archived for 15 years.

Your rights

In accordance with the provisions of the Règlement Général sur la Protection des Données (Règlement (UE) 2016/679)) and of the law "n°78-17 relative à l'informatique, aux fichiers et aux libertés", you have the following rights:

- The right to object: the right to object at any time to the transmission of your and your child's data. You can exercise this right to object to the data collected (i.e., you can refuse to answer the project questionnaires). To do so, you just have to inform the head of the school or the project referent.

- The right to withdraw, at any time, your agreement regarding the collection of your and your child's data. To do so, you will have to communicate the participant code to the head of the school or to the project referent; this is the only way to make the link between your data, you and your child. If during the course of the project you no longer wish to participate, your and your child's data collected before your withdrawal will nevertheless be used by the

investigator-coordinator in accordance with the public health code. Indeed, their deletion would compromise the achievement of the project's objectives.

- The right of access to information about you and your child, in order to verify their accuracy and, if necessary, to rectify, complete or update them.
- The right to restrict processing: right to block the use of your data and those of your child, no action can be performed on them.

You will be able to exercise your rights and those of your child by contacting the head of the school or the project referent and by providing them with your child's participant code.
In case of difficulty in exercising your rights or those of your child, you can also contact the Inserm Data Protection Officer by email (dpo@inserm.fr) or postal mail (Délégué à la Protection des Données de l'Inserm, 101 rue de Tolbiac, 75 013 Paris).
If you are unable to exercise your rights "Informatique et Libertés" as mentioned above or if you feel that your personal data has been violated, we inform you that you also have the right to file a complaint with the "Commission Nationale de l'Informatique et des Libertés - CNIL- l'autorité française de protection des données personnelles", 3 Place de Fontenoy - TSA 80715, 75334 PARIS CEDEX 07 or online at https://www.cnil.fr.

Below is a summary table.

Data controller	**Data processor**	**Data Protection Officer**	**Supervisory authority**
Who is responsible for the project?	*Who to contact to exercise your rights?*	*In case of difficulties to exercise your rights*	*To file a complaint*
Institut National de la Santé et de la Recherche Médicale (Inserm)	Head of your child's school, project referent	DPO Inserm	CNIL
101 rue de Tolbiac, 75 013 Paris	Project referent's name appears on the project label stuck in your child's home-school liaison booklet	101 rue de Tolbiac, 75 013 Paris dpo@inserm.fr	3 Place de Fontenoy, TSA 80715, 75 334 PARIS CEDEX 07 https://www.cnil.fr

5. INFORMATION ON THE OVERALL RESULTS

You have the right to be informed of the overall results of this project. To do so, you can contact the head of the school or the project referent.
The results of this project can be presented during conferences or in scientific publications.
As no information allowing you to be identified is collected, your child's name and surname or your own will not be published.

6. LEGISLATIVE AND REGULATORY PROVISIONS

This project is carried out in accordance with the applicable regulations[3]. It was approved by the Comité de Protection des Personnes « SUD-EST VI » on 22/12/2020.

It was approved by the Commission Nationale de l'Informatique et des Libertés (CNIL) (reference 921334) on 26/10/2021.

Thank you for taking the time to read this information sheet.

[3]Articles L.1121-1 and following of the public health code, relating to research involving the human person.

Bocquier A, *et al. BMJ Open* 2022; 12:e057943. doi: 10.1136/bmjopen-2021-057943

B) Adolescents' information sheet (for groups 1 and 3)

ADOLESCENTS' INFORMATION SHEET

Version N°**4.0 07/10/2021**

N° Inserm	N°IDRCB	N° CPP	N°CNIL
C20-76	2020-A02031-38	AU 1655	921334

Your secondary school participates in the PrevHPV project ("Evaluation of a multicomponent intervention aiming at improving the acceptability of Human Papillomavirus (HPV) vaccination in France") coordinated by Pr Nathalie THILLY, investigator-coordinator[4] of this project.

The PrevHPV project is conducted by 8 research teams with expertise in Epidemiology, Social and Human Sciences and Primary Care. It is a multicentre study, i.e., conducted in several secondary schools in France.

This project is also supported by the Direction Générale de l'Enseignement Scolaire (DGESCO).

The purpose of this document is to give you written information to help you decide whether or not you will participate in this project. You are free to participate or not. During the course of the project, if you need additional information, do not hesitate to ask questions to the head of your school or to the project referent (whose name appears on the project label stuck in your home-school liaison booklet).

The Inserm, Institut National de la Santé et de la Recherche Médicale, is the sponsor[5] of this project (*Inserm - Pôle Clinique – Biopark, Bâtiment A 8 rue de la Croix Jarry 75013 Paris*).

1. CONTEXT, OBJECTIVES AND JUSTIFICATION

HPV infection is the most common viral infection of the reproductive tract worldwide.

It is associated with an increased risk of some cancers (cervix, vagina, vulva, penis, anus and oropharynx) among women and men.

Vaccination against HPV has been available for more than 10 years. It is effective against 90% of the HPV infections responsible for cancers and also protects against anogenital warts (also called condylomas).

Until 2019, vaccination was mainly recommended for young girls, but despite many reassuring data on the effectiveness and safety of the vaccine, less than 30% of girls aged 11 to 14 years are vaccinated in France.

In order to better fight this virus, as of December 16, 2019, it was decided to recommend the vaccine for boys aged 11 to 14 years too.

The aim of the PrevHPV project is to propose the implementation of different actions within secondary schools and to observe whether these actions allow increasing the number of vaccinated adolescents (girls and boys aged 11-14).

[4] The investigator is the person responsible for the conduct of the research at a trial site. If the research involves several investigators, one investigator-coordinator is appointed among them.

[5] The sponsor is an individual, company, institution, or organization which takes responsibility for the initiation, management, and/or financing of a trial.

2. DESCRIPTION OF THE PROJECT

As part of the PrevHPV project, the intervention includes different actions that will be carried out within your school:

- First, you will be asked to **complete an online questionnaire during class hours**. This step will take 15 minutes. This questionnaire aims at assessing your knowledge and perceptions about HPV infection and vaccination. *(This first questionnaire will be provided soon.)*

- Then, some educational sessions on HPV infections and vaccination (entitled "Education, Motivation and Mobilisation") will be proposed as part of the school curriculum. These sessions will be performed during class hours, specifically for pupils in grades 9th and 10th). **During these sessions, some specific tools developed as part of this project (serious game, videos…) will be used. You will be asked whether or not you found these tools appropriate.**
  (Your parents will also be invited to information meetings on this topic and will be able to ask questions on it).

Then, if you have not yet been vaccinated, you will be able to get vaccinated against HPV directly at school during a day dedicated to vaccination. During this day, a physician and a nurse, working in a vaccination centre and used to vaccinate, will be present to vaccinate the teenagers whose parents (holders of the parental authority) have given their written consent. The project referent of your school will give you additional information on this intervention conducted by the vaccination centre soon. You and your parents are free to accept or refuse this vaccination. And, if you want to get vaccinated but not at school, you and your parents can refer to your general practitioner (or any other health professional of your choice). After the vaccination at school, we will ask you to complete a questionnaire of satisfaction about the action performed by the vaccination centre.

- Lastly, you will be asked to **complete another online questionnaire during class hours**. This step will take 15 minutes. This questionnaire aims at assessing whether your knowledge and perceptions about HPV infection and vaccination have changed since the beginning of the intervention.

For all participating municipalities, the number of vaccinated and unvaccinated adolescents aged 11-14 years will be collected using data from the Système National des Données de Santé (anonymous data on vaccines delivered in community pharmacies) and from vaccination and family planning centres (also anonymous data). These data will be collected before the intervention and then 2 months, 6 months and 12 months after the end of the intervention. These data will allow us to measure the impact of our project on the percentage of adolescents vaccinated against HPV.

Duration of your participation: 6 months
Total duration of the project: 6 years

3. EXPECTED BENEFITS, CONSTRAINTS, RISKS AND SPECIFIC PROJECT PROCEDURES

There is no risk associated with participating in this project.

Your participation is voluntary. If you do not want to answer the questionnaires during school hours, you just have to inform the head of the school or the project referent, whose name appears on the project label stuck in your home-school liaison booklet.

The results of this project will allow a better understanding of vaccination preferences from a scientific research perspective. These data can then help increase vaccination coverage in France and decrease the number of HPV-related infections in the population.

For more information on HPV and/or HPV vaccination you can contact your general practitioner or visit the website https://vaccination-info-service.fr/

4. CONFIDENTIALITY AND PROCESSING OF YOUR PERSONAL DATA

As part of this project, the processing of your personal data (in particular your age, sex, school municipality) will be performed to enable the analysis of the research's results. The execution of the public interest mission entrusted to Inserm justifies the processing of your personal data for scientific research purposes. The collected data will not be directly identifying. These data will be identified by a non-identifying confidential number (participant code) which you will receive and be the only one able to enter. There will be no correspondence between this participant code and your identity.

How long your data will be retained and archived as part of this project:

The data collected through the questionnaires will be analysed by the PrevHPV teams under the responsibility of the investigator-coordinator.

Your data will be kept in the secure information systems of the PrevHPV consortium's data controller for a maximum of 7 years (duration of the project + 1 year necessary for the writing of the final report). Then, the data will be archived for 15 years.

Your rights

In accordance with the provisions of the Règlement Général sur la Protection des Données (Règlement (UE) 2016/679)) and of the law "n°78-17 relative à l'informatique, aux fichiers et aux libertés", you have the following rights:

- The right to object: the right to object at any time to the transmission of your data. You can exercise this right to object to the data collected (i.e., you can refuse to answer the project questionnaires). To do so, you just have to inform the head of the school or the project referent.
- The right to withdraw, at any time, your agreement regarding the collection of your data. To do so, you will have to communicate the participant code to the head of the school or to the project referent; this is the only way to make the link between your data and you. If during the course of the project you no longer wish to participate, your data collected before your withdrawal will nevertheless be used by the investigator-coordinator in accordance with the public health code. Indeed, their deletion would compromise the achievement of the project's objectives.
- The right of access to information about you, in order to verify their accuracy and, if necessary, to rectify, complete or update them.

- The right to restrict processing: right to block the use of your data, no action can be performed on them.

Your parents will be able to exercise your rights by contacting the head of the school or the project referent and by providing them with your participant code.

In case of difficulty in exercising your rights, your parents can also contact the Inserm Data Protection Officer by email (dpo@inserm.fr) or postal mail (Délégué à la Protection des Données de l'Inserm, 101 rue de Tolbiac, 75 013 Paris).

If you are unable to exercise your rights "Informatique et Libertés" as mentioned above or if you feel that your personal data has been violated, we inform you that you also have the right to file a complaint with the "Commission Nationale de l'Informatique et des Libertés - CNIL- l'autorité française de protection des données personnelles", 3 Place de Fontenoy - TSA 80715, 75334 PARIS CEDEX 07 or online at https://www.cnil.fr.

Below is a summary table.

Data controller	**Data processor**	**Data Protection Officer**	**Supervisory authority**
Who is responsible for the project?	*Who to contact to exercise your rights?*	*In case of difficulties to exercise your rights*	*To file a complaint*
Institut National de la Santé et de la Recherche Médicale (Inserm)	Head of the school, project referent	DPO Inserm	CNIL
101 rue de Tolbiac, 75 013 Paris	Project referent's name appears on the project label stuck in your home-school liaison booklet	101 rue de Tolbiac, 75 013 Paris dpo@inserm.fr	3 Place de Fontenoy, TSA 80715, 75334 PARIS CEDEX 07 https://www.cnil.fr

5. INFORMATION ON THE OVERALL RESULTS

You have the right to be informed of the overall results of this project. To do so, you can contact the head of the school or the project referent.

The results of this project can be presented during conferences or in scientific publications.

As no information allowing you to be identified is collected, your child's name and surname or your own will not be published.

6. LEGISLATIVE AND REGULATORY PROVISIONS

This project is carried out in accordance with the applicable regulations[6]. It was approved by the Comité de Protection des Personnes « SUD-EST VI » on 22/12/2020.

It was approved by the Commission Nationale de l'Informatique et des Libertés (CNIL) (reference 921334) on 26/10/2021.

Thank you for taking the time to read this information sheet.

[6]Articles L.1121-1 and following of the public health code, relating to research involving the human person.

C) General practitioners' information sheet

GENERAL PRACTITIONNERS' INFORMATION SHEET

Version N°**5.0 07/10/2021**

N° Inserm	N°IDRCB	N° CPP	N°CNIL
C20-76	2020-A02031-38	AU 1655	921334

Dear colleague,

The "Département de Médecine Générale" of the Université de Paris (Pr Serge Gilberg) participates in the PrevHPV project ("Evaluation of a multicomponent intervention aiming at improving the acceptability of Human Papillomavirus (HPV) vaccination in France") coordinated by Pr Nathalie THILLY, investigator-coordinator[7] of this project.

The PrevHPV project is conducted by 8 research teams with expertise in Epidemiology, Social and Human Sciences and Primary Care. It is a multicentre study, i.e., conducted in several secondary schools in France.

This project is also supported by the Direction Générale de l'Enseignement Scolaire (DGESCO).

The purpose of this document is to give you written information to help you understand the project and decide whether or not you will participate in this project. You are free to participate or not.

The Inserm, Institut National de la Santé et de la Recherche Médicale, is the sponsor[8] of this project (*Inserm - Pôle Clinique – Biopark, Bâtiment A 8 rue de la Croix Jarry 75013 Paris*).

1. CONTEXT, OBJECTIVES AND JUSTIFICATION

HPV infection is the most common viral infection of the reproductive tract worldwide.

It is associated with an increased risk of some cancers (cervix, vagina, vulva, penis, anus and oropharynx) among women and men.

Vaccination against HPV has been available for more than 10 years. It is effective against 90% of the HPV infections responsible for cancers and also protects against anogenital warts.

Until 2019, vaccination was mainly recommended for young girls, but despite many reassuring data on the effectiveness and safety of the vaccine, the vaccine coverage in France remains one of the lowest in Europe; it is lower than 30% among girls aged 11 to 14 years.

Since December 16, 2019, the Haute Autorité de Santé (HAS) has recommended the expansion of the vaccination to boys aged 11-14 years (universal vaccination).

This project aims at improving the acceptability of HPV vaccination in France. To that purpose, the PrevHPV teams will perform actions in secondary schools and one action among general practitioners.

[7] The investigator is the person responsible for the conduct of the research at a trial site. If the research involves several investigators, one investigator-coordinator is appointed among them.

[8] The sponsor is an individual, company, institution, or organization which takes responsibility for the initiation, management, and/or financing of a trial.

These actions are the following:

1. **'Education, Motivation, Mobilisation'** targeting adolescents and their parents and aiming at information/educating on HPV infections and vaccination;
2. **'HPV vaccination at school'** which consists of a vaccination day on school premises where health professionals from local vaccination centres initiate HPV vaccination;
3. **'General practitioners' training'** with a training on the use of motivational interviewing techniques in the field of vaccination and provision of an educational tool to support the dialogue necessary for parents to make an informed decision to vaccinate an adolescent.

Indeed, in the context of vaccination in general, general practitioners play a key role, but to date have only been rarely targeted in actions aimed at improving vaccination coverage. Every day, we, general practitioners, face vaccine hesitancy and because of our proximity to young people and their parents, we are a significant source of information and can help them in their decision making.

2. DESCRIPTION OF THE PROJECT

You are located in a municipality where we are evaluating the effect on vaccination coverage of training for general practitioners and in order to be able to invite you to participate in the PrevHPV project, we have used the public contact information available in the "pages jaunes" and the "Conseil National de l'Ordre des Médecins" directories.

We offer you, if you wish, access to our training modules on HPV and its vaccination, the technique of motivational interviewing in the field of vaccination and the use of a decision aid tool that will be made available to you and that you can use afterwards.

This is an **online training which lasted about 3 hours** and **composed of 4 modules that you can follow according to your availability (and by stopping and starting again at any time)**.

If you agree to follow the proposed training, **we will also ask you to complete 2 online questionnaires, one at the beginning of the training and the second at the end of the training (about 5 minutes per questionnaire) on your activity and your practices regarding PrevHPV vaccination. A compensation of 350€ is available for the general practitioners who have followed the training and completed the 2 questionnaires.**

If you do not wish to participate, we simply ask you to inform us.

If you agree to participate, you may withdraw at any time without incurring any liability or prejudice. We will simply ask you to inform us.

From now on and throughout the duration of your participation, if you need additional information, you can contact the team of **Pr Gilberg Serge by contacting the PrevHPV Project Manager**:

Mme Minghui ZUO

07 81 92 47 23 - minghui.zuo@parisdescartes.fr

For all participating municipalities, the number of vaccinated and unvaccinated adolescents aged 11-14 years will be collected using data from the Système National des Données de Santé (anonymous data on vaccines delivered in community pharmacies) and from vaccination and family planning centres (also anonymous data). These data will be collected before the intervention and then 2 months, 6 months and 12 months after the end

of the intervention. These data will allow us to measure the impact of our project on the percentage of adolescents vaccinated against HPV.

Duration of your participation: 6 months
Total duration of the project: 6 years

3. EXPECTED BENEFICES, CONSTRAINTS, RISKS AND SPECIFIC PROJECT PROCEDURES

There is no risk associated with participating in this project.
The results of this research will help identify potentially effective actions to increase the acceptability of HPV vaccination, from a scientific research perspective. These data can then help increase vaccination coverage in France and decrease the number of HPV-related infections in the population.

4. CONFIDENTIALITY AND PROCESSING OF YOUR PERSONAL DATA

As part of this project, the processing of your personal data will be performed to monitor the progress of the project and enable the analysis of the research's results. The execution of the public interest mission entrusted to Inserm justifies the processing of your personal data for scientific research purposes.

The project manager of Pr Gilberg's team will provide you with a confidential non-identifying code to use when you complete the online questionnaire. The PrevHPV team in charge of analysing the questionnaires will not know your identity and will only know the confidential code.

How long your data will be retained and archived as part of this project:
The data collected through the questionnaires will be analysed by the PrevHPV teams under the responsibility of the investigator-coordinator.
Your data will be kept in the secure information systems of the PrevHPV consortium's data controller for a maximum of 7 years (duration of the project + 1 year necessary for the writing of the final report). Then, the data will be archived for 15 years.
Once the data has been collected and checked, the table of correspondence between your confidential code and your identity held by the "Université Paris - Département de Médecine Générale" during contacts with general practitioners throughout the project will be deleted (i.e., at the end of two years following the start of the intervention).

Your rights
In accordance with the provisions of the Règlement Général sur la Protection des Données (Règlement (UE) 2016/679)) and of the law "n°78-17 relative à l'informatique, aux fichiers et aux libertés", you have the following rights:

- The right to object: the right to object at any time to the transmission of your data and to the collection of your data in the future. You can exercice this right to object to data collected. For that, you just have to inform the Pr Gilberg's team (address above).
- The right to withdraw, at any time, your agreement regarding the collection of your data. If during the course of the project you no longer wish to participate, your data collected before your withdrawal will nevertheless be used by the investigator-coordinator or her representative

in accordance with the public health code. Indeed, their deletion would compromise the achievement of the project's objectives. For that, you just have to inform the Pr Gilberg's team.

- The right of access to information about you, in order to verify their accuracy and, if necessary, to rectify, complete or update them.
- The right to restrict processing: right to block the use of your data, no action can be performed on them.

You will be able to exercise your rights for 24 months after the start of the intervention. After that, the correspondence table between your participant code and your identity will be deleted. You will then have to communicate your participant code to exercise your rights, please keep it.

In case of difficulty in exercising your rights, you can also contact the Inserm Data Protection Officer by email (dpo@inserm.fr) or postal mail (Délégué à la Protection des Données de l'Inserm, 101 rue de Tolbiac, 75 013 Paris).

If you are unable to exercise your rights "Informatique et Libertés" as mentioned above or if you feel that your personal data has been violated, we inform you that you also have the right to file a complaint with the "Commission Nationale de l'Informatique et des Libertés - CNIL- l'autorité française de protection des données personnelles", 3 Place de Fontenoy - TSA 80715, 75334 PARIS CEDEX 07 or online at https://www.cnil.fr.

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Who is responsible for the project?	*Who to contact to exercise your rights?*	*In case of difficulties to exercise your rights*	*To file a complaint*
Institut National de la Santé et de la Recherche Médicale (Inserm)	Pr Gilberg's team	DPO Inserm	CNIL
101 rue de Tolbiac, 75 013 Paris	Département de Médecine Générale - Université Paris - 24 rue du Faubourg Saint-Jacques -75679 PARIS Cedex 14 01.44.41.23.63 sergegilberg@gmail.com	101 rue de Tolbiac, 75 013 Paris dpo@inserm.fr	3 Place de Fontenoy, TSA 80715, 75334 PARIS CEDEX 07 https://www.cnil.fr

5. INFORMATION ON THE OVERALL RESULTS

You have the right to be informed of the overall results of this project by contacting the Pr Gilberg's team.

The results of this project can be presented during conferences or in scientific publications.

Your data will be completely anonymous and you will not be identified. Your data will generally be aggregated with that of other participants in order to reach overall scientific conclusions.

6. LEGISLATIVES AND REGULATORY PROVISIONS

This project is carried out in accordance with the applicable regulations[9]. It was approved by the Comité de Protection des Personnes « SUD-EST VI » on 22/12/2020.

It was approved by the Commission Nationale de l'Informatique et des Libertés (CNIL) (reference 921334) on 26/10/2021.

Thank you for taking the time to read this information sheet.

[9]Articles L.1121-1 and following of the public health code, relating to research involving the human person.