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METHOD

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The community nurse's role on the promotion of papillomavirus vaccination among young students: A study protocol

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ABSTRACT

Vaccination is the principal strategy for primary prevention of infection by Human Papilloma Virus (HPV), which causes different pathological conditions, up to cancer, in both males and females. However, to date, knowledge among adolescents and their parents about the HPV vaccine is still low. The aim of this quasi-experimental, multicenter study is to assess the effectiveness of a digital educational intervention, conducted by a multidisciplinary health-care team including a Community Nurse, to increase adolescents' HPV vaccination uptake, their knowledge, self-efficacy, feelings and involvement in HPV vaccine decision-making, and parents' vaccination hesitancy. The study will be carried out among a population of students (and their parents), aged between 11 and 13, at secondary schools in Italy. Validated questionnaires will be administered to both students and parents at baseline (T0) and 3 months after a digital educational intervention (T1). The findings may be useful in evaluating and deepening a methodology for designing and implementing educational interventions, embedded in the school setting, that could promote the achievement of outcomes within the broader process of youth's health promotion.

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Introduction

Over the past 15 years, there has been an increase in vaccination coverage against Human Papillomavirus (HPV), which remains the most prevalent and is the leading cause of cervical cancers, in addition to vulvar, vaginal, anal, penile, and oral cancers, among sexually transmitted infections.[1] In 2012, there were 67,355 new cases of cervical cancer in Europe (age-standardized incidence rate of 11.2 per 100,000 women) and 28,003 deaths related to this disease (age-standardized mortality rate of 3.8 per 100,000), leading to a serious impact on the quality of life of affected women[2] and the financial burden caused by this infection. In Italy, in 2018, the annual direct costs related to cervical cancer treatment ranged from 346.7 to 782.0 million euros. These costs could also increase when considering innovative cancer therapies.[3] Within cervical cancer prophylaxis programs, recent evidence suggests primary and secondary preventions as cost-effective.[4] Among current vaccines, nonavalent (Gardasil9) prevents about the 90% of cervical, vulvar, vaginal, and anal cancers.[5]

Background

As of 2019, as many as 100 countries around the world, including Italy, offer HPV vaccination as part of the regular immunization plan to eradicate cervical cancer, as it is considered a major public health problem.[6]

To date, both male and female vaccine programs at an early age (youth and adolescents) and in adults appear to be able to reduce the incidence of HPV infections, genital condylomas, and precancerous lesions attributed to HPV.[7] The benefits of vaccination are also tangible from an economic point of view for Health Systems, as evidenced by a study[8] conducted in Italy, where a clear reduction in hospitalization costs (39%) was observed 9 years after the introduction of preventive measures (screening and vaccines).

In Italy, free HPV vaccination is guaranteed for all adolescents (males and females) between the ages of 11–12 years,[9] before the age of possible infection, and when the immune response is best, and the benefit is greatest. However, since these are underage, parental consent is required and, currently, the national coverage is low compared to other vaccinations. Average HPV vaccination coverage in both girls and boys is below the optimal threshold identified by the National Vaccine Prevention Plan (95% in the 12th year of life), and the national program is far from achieving the 95% coverage.[10] In Italy, HPV vaccination coverage in girls and boys, already far from the 95% target in previous years, was further reduced in 2020 (2008 birth cohort), due to the strong impact of the pandemic on vaccination activities. For the target population of 15-year old for 2020 it was 63.8% compared to 70.3% in 2019.[11]

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Worldwide, most national HPV vaccination programs include only girls. However, "gender-neutral" vaccinations are increasingly considered important from a "cost-effectiveness" perspective to prevent cancer[12] and are recommended by several countries such as Australia, Austria, Barbados, Israel, Liechtenstein, Switzerland, the United States of America (U.S.A.), Canada,[13] and Italy.[14]

However, knowledge among adolescents and their parents about the virus and the HPV vaccine is low, and there is a lack of awareness about the benefits of vaccination in males.[15] In Italy, for males it is even worse with percentages of fully vaccinated people of 24.17% in 2020 compared to 32, 25% in 2019. Furthermore, there is a wide variability in vaccination rates between Italian regions, especially in Southern Italy, where vaccination rates are decreasing.[11]

In Italy, in relation to the objective set by the State-Regions Agreement, it is recognized the importance to regularly monitor vaccination coverage data, to promptly identify areas of low coverage. Furthermore, considering the sensitivity of the topic and the complex message to be conveyed to the target audience and their families on this vaccination, the communication aspects of the campaign are of crucial importance. It is fundamental to find the right channel of communication, in relation to a specific target of population. To articulate and make communication more effective, it is advisable to involve multidisciplinary health-care teams and educational institutions, as schools, supporting Regions and Local Health Authorities in the vaccination campaigns against HPV, with the aim of increasing vaccination coverage for this infection throughout the national territory.[16] This ambitious objective can be achieved starting from a local context, to test the effectiveness of an educational intervention, specifically tailored for adolescents and their families.

As of today, experimental or quasi-experimental studies with the aim of testing the effectiveness of an educational intervention regarding papillomavirus are mostly aimed at adolescents attending secondary schools (14–19 years old),[17] even though vaccination is recommended in the 11–12 age group. Also, even though school-based vaccination programs are considered traditional and effective strategies to promote HPV vaccination, they could face several obstacles, including undervaluation, misunderstanding, attitudinal barriers, structural barriers such as scheduling challenges, and expensive incentives. Digital interventions leveraging technology and online platforms offer solutions to these challenges.[18]

In fact, among the most innovative and effective ways to deliver health education interventions, digital communication through information and communication technologies (ICTs) is the best strategy to support citizens because it provides them with the tools to become independent and responsible actors, able to choose voluntarily and consciously to adhere to vaccination programs.[19] In particular, a recent systematic review and meta-analysis reported how some digital interventions targeting male or mixed-gender participants demonstrate greater benefit, and reminder platforms (SMS, preference reminders, or electronic health record alerts) were more effective in increasing HPV vaccination rates.[18]

However, there have been no school-based interventional studies aimed at increasing HPV vaccination rates by making use of digital and involving all stakeholders within this process: community nurses, physicians, parents, and adolescents, according to the principles of patient and public involvement (PPI).

Aims

The primary aim of the study is to identify the effectiveness of a digital educational intervention, conducted by a multidisciplinary health-care team and targeting adolescents of both sexes in secondary schools.

The primary outcome measures will be to evaluate (i) vaccination uptake, (ii) self-efficacy, (iii) feelings (fear and anxiety), (iv) involvement in vaccine decision-making, pre-post intervention.

The secondary aim is to evaluate parents' hesitancy toward vaccination pre- and post-educational intervention.

Method

Design

A multicenter, quasi-experimental, pre-post educational intervention study will be conducted from February 2023 to August 2024. This protocol was registered in the ClinicalTrials.gov, with identification number NCT05485441.

Based on previous studies evaluating the effectiveness of co-produced educational packages and interventions for school-based HPV vaccination programs,[20,21] in this study will consider a combined approach enclosing the review of current evidence, Patient and Public Involvement (PPI) activities and multi-disciplinary team input in developing the intervention. The PPI activities will preliminarily inform each phase of the project (Figure 1).

Study setting and sampling

Convenience sampling will be adopted at secondary schools *in the province of Bari (Apulia region, south-eastern Italy)*.

To properly test the instruments' reliability and validity, it is recommended to recruit from 5 to 20 participants per item.[22] Considering 15 items of the parents' scale and 25 items for students' scale the final sample size will be comprised between 75 and 300 participants.

To determine the effect of the intervention tested, we consider an accessible population of 34,951 students between the ages of 11 and 13 in the area and related 69,902 parents.[23]

In precautionary terms, a dropout of 20% of the initial sample is expected. Given these variables, a 5% margin of error and a 95% confidence interval, the expected sample size is 380 for students and 383 for parents. Sample size was calculated using G*Power version 3.1.9.7.[24]

Inclusion and exclusion criteria

All parents and students enrolled in Year I, II, III of the 2022/2023 and 2023/2024 school year between the ages of 11 and 13 will be included. Individuals with disabilities, with visual and

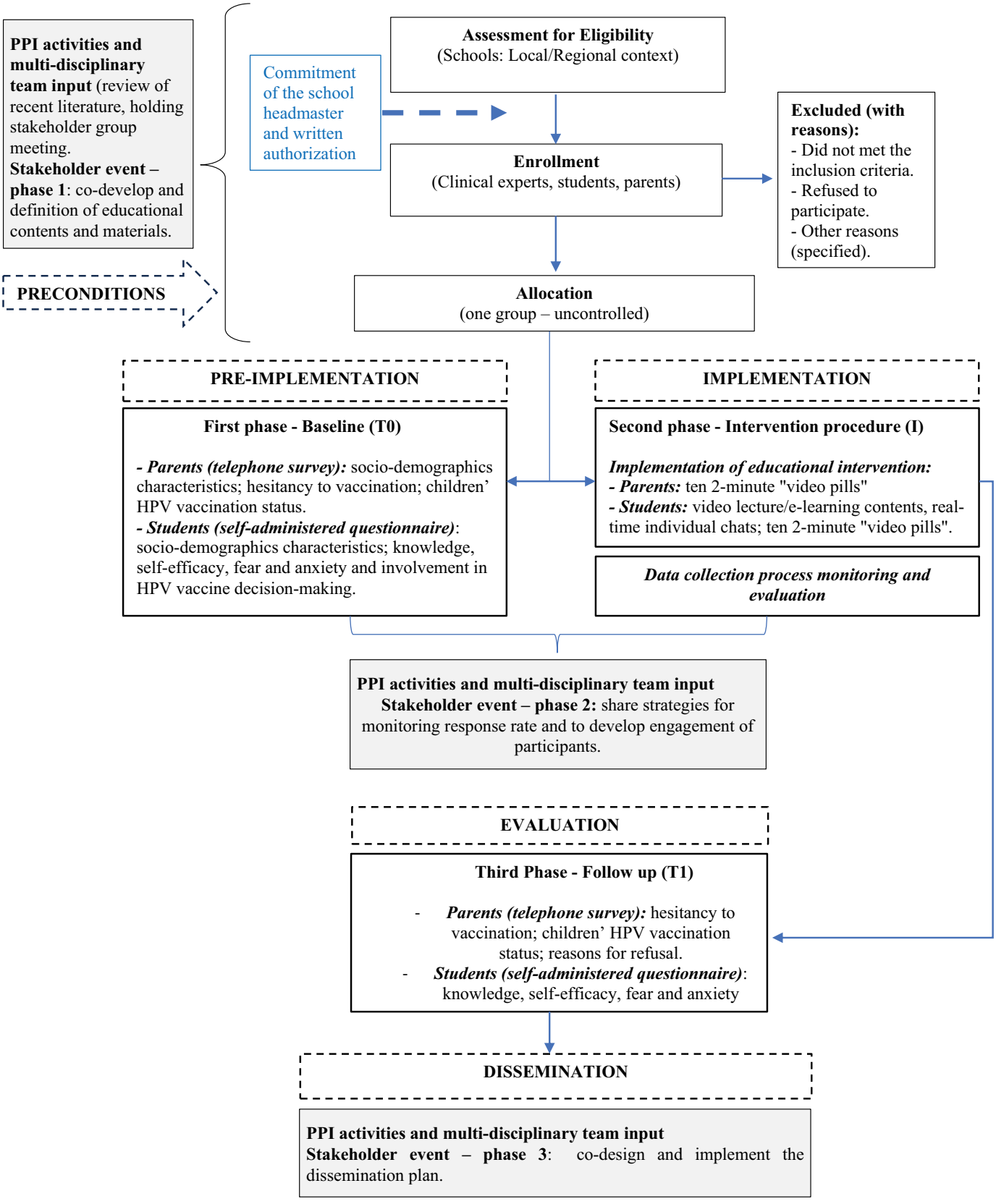

Figure 1. Flow diagram of the intervention study.

hearing impairment, will be able to participate in the educational intervention supported by their support teacher.

Those who do not agree to participate, who do not provide informed consent as well as a telephone number and e-mail address to be contacted, will be excluded.

Data collection

Prior to the start of the study, at each data collection center, it will be required to obtain the commitment of the school headmaster and written authorization for data collection from the

facility and the child's parents/legal guardians. Community Nurses previously identified based on the specialized training acquired (master's degree in: Family and Community Nursing or in Hygiene and Public Health or regional courses on specific training in territorial settings), will enroll participants matching the recruitment criteria.

Parents and students will be asked to complete their instruments of data collection at two time points: at baseline (T0) and 3 months after educational intervention (T1)

First phase - baseline (T0)

Prior to the educational intervention, a baseline survey will be performed to assess parents' and students' socio-demographics characteristics; students' HPV vaccination status, their knowledge, self-efficacy, fear and anxiety and involvement in HPV vaccine decision-making, parents' hesitancy to vaccination.

Upon prior arrangement with the school Principal and after receiving a list of agreement of study participants (of both parents and students) the Community Nurse will collect the parents' baseline assessment through a telephone survey of lasting 15 min.

Students' baseline information will be collected at school directly by the Community Nurse in a self-administered manner.

Second phase - intervention procedure (I)

After completion of the baseline assessment, the Community Nurse will set up an educational intervention, involving two members of the panel of experts for each school (Community Nurse and physician) with expertise in public health. The intervention will take place only when a minimum number of 20 participants is reached in each of the participating schools.

Description of the educational intervention

The educational intervention (I) will be provided in two ways: (I) a video lecture in e-learning mode lasting about an hour, aimed at adolescents, using the School Institute's platform for distance education, using audiovisual systems and slide presentations in Power Point format; learner–learner interactions will be possible through real-time individual chats.

The e-learning content will be screen at school, during the supplementary lesson dedicated to the educational event and will cover the following topic areas: a) basic information on HPV, modes of prevention and contagion, vaccination, and sexual health; b) epidemiology on cervical cancer, incidence, and mortality rates; c) preventive measures (vaccines, condoms, screening tests) and d) discussion with privileged witnesses who have experienced contagion. No form of clinical counseling will be carried out during the video lectures.

(II) The second way will consist in the promotion of 2-min "video pills," available to users (students and their parents) delivered through schools' social channels, in which four clinical experts of the panel (pediatrician, hygienist, health-care assistant, and Community Nurse) will raise awareness of the importance of HPV vaccination in adolescents. A total of 10 "Video pills" will be reordered providing brief information on the following themes: (i) modes of virus transmission (three videos), (ii) prevention (three videos), and (iii) health effects of the virus (four videos). Both students and parents will have the possibility to watch "Video pills" at their personal convenience, after registering on the school portal channel to certify their online activity.

Third phase - follow up (T1)

In the last phase (3 months after the intervention), an in-person (for students) and a telephone interview (for parents) will be conducted by the Community Nurse, to collect the same information of baseline, except for socio-demographic data.

In particular, students' vaccination uptake rate after the educational intervention and reasons for eventual refusal will be assessed by offering participants the same series of preset responses included in the "Information on vaccination status" section administered to parents at the baseline (T0).

Outcomes and measurement

The primary outcomes are students' HPV vaccination uptake, students' knowledge, self-efficacy, fear and anxiety, and involvement in HPV vaccine decision-making. The secondary outcome is parents' HPV vaccine hesitancy.

Outcomes will be determined at 3 months (T1) after the educational intervention by the Community Nurse.

Sociodemographic characteristics

Questionnaire to students: school, gender (at birth), age, nationality, religious orientation, history of sexual experiences (single-item measures: "Have you ever had sexual experiences?"; response variables: yes, no, I prefer not to answer).

Questionnaire to parents: gender, marital status, age, religious orientation, educational level, number and age of their children (date of birth), family history of cancer cases (single-item measures: "Do you have a family history of cancer?"; response variables: yes, no, I prefer not to answer).

Immunization status

After sociodemographic section of the parents 'questionnaire, vaccination status of students and their delayed adherence to or refusal to vaccinate for HPV, diphtheria, hepatitis B, Haemophilus influenzae type B, measles, parotitis, polio, rubella, tetanus, and varicella will be reported in the section "information on vaccination status." For each of the vaccine listed above, we used single-item measures for delay: "Have you ever delayed having your child get a shot of vaccine?," response variables: yes, no, I do not know; and single-item measures for refusal: "Have you ever refused having your child get a shot of vaccine?," response variables: yes, no, I do not know.

We will also record the reasons for having delayed vaccinations (forgetfulness, vaccine not-available in the vaccination center, concerns about side effects, fear of the vaccine administration for their children, lack of recommendation by the Pediatricians) and reasons for having refused vaccinations (lack of recommendation by the pediatricians, having an objection to the administration of the vaccines, forgetfulness, concerns about side effects, vaccine not available in the vaccination center).

Students' knowledge, self-efficacy, fear and anxiety, involvement in HPV vaccine decision making

Students' HPV Adolescent Vaccine Intervention Questionnaire (HAVIQ)[25] a multidimensional questionnaire consisting of 25 items will be used to measure the following dimensions: (I) students' involvement in vaccine decision-making (8 items), (II) HPV self-efficacy "Skills inventory (certainty)" (5 items), (III) feelings (fear and anxiety) toward vaccination (6 items), (IV) HPV and HPV vaccine knowledge (6 items). The dimensions I, III, and IV of HAVIQ are measured with different questions, each rated on a 5-points Likert scale ranging from "strongly disagree" to "strongly agree." Whereas "Skills inventory (certainty)" rates from 0 to 100 by using a confidence scale (from "cannot to at all" to "highly certain can do").

The knowledge questions were supplemented by 10 items with dichotomous "yes/no" responses.[15] The total score ranges from 0 (no knowledge) to 10 (highest level of knowledge).

The questionnaire was authorized for its use by the authors[25] and underwent a backward-forward translation process for content validity and then tested on a sample of 25 students.

Parents' hesitancy to HPV vaccination

Parents' hesitancy to vaccine their children toward HPV will be measured through the Italian version[26] of the Parent Attitudes about Childhood Vaccines Survey (PACV) by Opel and colleagues,[27–29] a validated tool to identify vaccine-hesitant parents, which consists of 15 items divided into three domains: behaviors, beliefs, attitudes, and general confidence about the efficacy and safety of vaccines.

Following the scoring modes used in the literature, the different PACV response modes (dichotomous, 5-point Likert scale and 10-point Likert scale) will be summarized into three response categories: (1) hesitant, (2) not sure, and (3) not hesitant. "Hesitant" responses will get a score of 2, "not sure or don't know" a score of 1, and "not hesitant" 0. In line with previous studies, we transformed the total score obtained into a scale from 0 to 100 by applying a simple linear transformation by dichotomizing the total PACV score generated, with a score < 50 indicating non-hesitant and ≥ 50 indicating hesitant. The total score ranges from 0 to 100: a parent is considered non-hesitant if he or she scores < 50 and hesitant with a value of ≥ 50.

Data analysis

The data will be analyzed with Stata v12.[30] Multivariate outliers and missing data in the distribution will be analyzed with the "bacon" package in Stata v12[31] and Little's Missing Completely at Random (MCAR) test to determine the random nature of missing data,[32] respectively. The multivariate normality of the distribution will be checked by calculating Mardia's kurtosis coefficient.[33]

Comparison of the pre- and post-intervention mean scores will be tested by the t-test with a significance limit of $p < .05$.

Reliability of instruments

The reliability of the adopted instruments will be checked by adopting Cronbach's alpha coefficient: values > .90 are considered excellent, between >0.70 and <0.90 good, between >0.60 and <0.70 acceptable and values <0.60 not acceptable.[34] Confirmatory factor analysis (CFA) will be carried out to verify the validity of the scales, and the corresponding fit indices will be calculated, the same will be considered acceptable based on the following criteria: RMSEA (root mean square error of approximation) and SRMR (standardized root mean residual) <0.08, CFI (comparative fit index), and TLI (Tucker-Lewis Index) >0.90.[22]

Ethical considerations

The study was approved by the Ethics Committee "Comitato Etico Indipendente – AOU "Consorziale Policlinico" of Bari with the following approval number: 2023–7581/0015620| 16/02/2023. No health information or patient data will be registered during this research project. However, the proposed project follows the current ethical guidelines for good practice in research and education. All project participants will be recruited on a voluntary basis, and informed consent will be obtained. All data will be anonymized and securely stored.

Informed consent

The study will commence after the signing of the "informed consent to voluntary participation in the study" and "consent to the processing of personal data" by the parents or, in their absence, by the legal guardian of adolescents, as well as the adolescent's verbal consent, in accordance with the Regulation (EU) 2016/679.[35]

Participant withdrawal

Participants will be able to withdraw at any time during the study, and the reasons for withdrawal will be recorded by the researchers. If a participant wishes to discontinue, data collection up to that point will be considered and appropriately managed in the analysis.

Confidentiality and storage of data

All participants' data collected will be kept confidential. For data management, the personal identification information of the participants will be replaced with identification numbers (ID)/codes. Personal data of participants useful to trace participants when needed (contact details, for example e-mail address and telephone number) will be collected and kept in a separate file from the research data, and it will be stored separately, with limited access. However, all personal information that could identify participants will be removed in order to guarantee anonymity before the results' dissemination. Findings will be reported only in aggregate form or in a manner that will not allow the identification of individual responses. Databases including all participants' data will be password-protected and

exclusively managed by researchers. All study data will be stored on the university password protected server. All documents (hard copies) will be stored in a secure filing cabinet at the university (locked rooms or cabinets with access limited to researchers) only accessible to the authorized research staff.

Status and timeline of the study

The study protocol has been submitted and approved by the Local Independent Ethical Committee of the Polyclinic of Bari. An overview of the operational timing planned is designed according to the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) guidelines[36] as shown in Figure 2.

	STUDY PERIOD-19 months							
	Enrolment	**Allocation**	**Post-allocation**					**Close-out**
TIMEPOINT**	***Feb.2023 Sept.2023***	**Oct.2023**	***Nov. 2023***	***Dec.2 023***	***Jan.2 024***	***Feb.2 024***	***May 2024***	***Jul.2024***
ENROLMENT:								
Eligibility of schools, enrollment clinical experts', content and platforms useful for deliver the digital intervention	X							
Definition of the educational project and materials and customization of digital platforms	X							
Clinical experts' enrollment; design of "videopills"	X							
Participants' enrollment (students and their parents)	X							
Allocation		X						
INTERVENTIONS								
(T0) Administration questionnaires: knowledge about HPV vaccination, involvement in vaccine decision-making, HPV vaccination situation			X					
(I) educational digital intervention to improve HPV knowledge and rate vaccination				X	X	X		
T1 Assess rate vaccination for HPV by administering the same instruments used at T0.							X	
Data analysis: T0, I and T1 (pre-post intervention) and dissemination of results								X
ASSESSMENTS:								
HPV Adolescent Vaccine Intervention Questionnaire			X				X	
Parent Attitudes about Childhood Vaccines Survey			X				X	

Figure 2. SPIRIT schedule.

Patient and public involvement

PPI activities are planned to co-design the educational contents of the intervention, the data collection strategies, and the dissemination activities of the core outcomes of this study, in accordance with the current guidelines and research recommendations for interventional studies.[37,38] PPI will preliminarily support this project by providing an enhanced fit of the research activities to the target population. The plan involves a representative panel of stakeholders (e.g., teachers, parents, and adolescents) by holding group meetings. The group will meet a minimum of three times a year in stakeholder events (phases 1, 2, and 3). In the Stakeholder event – phase 1, panel members will collaborate to co-develop and define the educational content of the intervention; in the Stakeholder event – phase 2, researchers and panel members will co-design strategies to monitor the response rate and, if necessary, to develop strategies to improve it; in the Stakeholder – phase 3, panel members will co-design the dissemination plan in order to better reach the target population and deliver the core outcomes of this study. They will define collaborative co-designed strategies to facilitate collection of adolescents/parents and health-care professionals' views, useful to inform dissemination planning. Each PPI meeting will be held before starting each phase of the research project and will inform the researchers in order to integrate the stakeholders' perspective in the research activities.

Communication between team members will be improved through a quarterly update of the study, following the first scheduled meeting; team members will be asked to hold virtual meetings to encourage team reflection, sharing ideas and sharing updates on study design setup and progress reports.

Discussion

This project will promote the implementation of new educational programs involving the use of digital technologies to improve the HPV vaccination uptake, knowledge, self-efficacy, feelings, and involvement in HPV vaccine decision-making among students aged 11–13 of both sexes and to improve their parents' vaccination hesitancy. Parental consent is required for vaccination, including HPV vaccination, in most countries worldwide; if parents were better informed, they may facilitate vaccination easier and thus raise vaccination uptake. However, to improve children/adolescents' understanding and knowledge regarding vaccination may increase their self-awareness and autonomy in vaccination decision-making,[39] also as future young adults. Moreover, to also involve children and adolescents in vaccination decision-making is one of the challenges facing the Health Systems.[39] In fact, some countries (i.e., the United Kingdom) have already introduced self-consent procedures for adolescents, to promote their active role in the decision-making process about HPV vaccination, based on considerations regarding their level of maturity and autonomy in health choices.[20,40]

Our outcomes have the potential to re-design the models to take in charge of the public health needs of the population and to address the future challenges of the healthcare system. The focus on communication and educational modalities to support vaccination decision-making is aimed at a target audience that is not purely pediatric but pre-adolescent, in which active involvement is a necessary strategy even though parental decision-making is still decisive in the final decision to adhere to vaccination. Moreover, this vaccination prevents a sexually transmitted infection and a cancer pathology that could occur years after the infection. Therefore, it is necessary to act early to protect the health of children/adolescents from the age of 11.

This project will promote positive outcomes on individual decision-making with respect to vaccination adherence, considering that (I) the use of digital tools as a mode of active involvement and education, which allow, for students aged between 11 and 13 to interact confidentially with educational channels appropriate to their mode of relationship and communication; (II) the reliability and competence of the source of information/education.

The decision not to adhere to HPV vaccination may also result from a lack of knowledge on the topic and not from a real and conscious volition not to vaccinate. In this context, a multi-professional educational intervention led by the healthcare professionals, and the Community Nurse, is aimed to foster in parents and their children a positive perception with respect to the sources of information, which, therefore, would be recognized as reliable and trustworthy.

Analyzing the effectiveness of the interventions proposed in this project may promote the development of an educational culture based on multi-professional collaboration and the development of an active network between health professionals and the school environment capable of proposing interventions within the community and about HPV vaccination, within schools. Indeed, it is the school where every individual, from the earliest years of life, can be educated to develop his or her own critical thinking oriented toward the adoption of health-promoting behaviors.

The results of this project, therefore, may be useful in evaluating and deepening a methodology for designing and implementing educational interventions, embedded in a system that considers communication as a structured and continuous process.

In this context, providing for systematically organized educational events embedded in the school setting promotes the achievement of outcomes related to the broader process of youth health promotion.

Strengths and limitations of the study

Evidence supports school-based education programs as effective interventions to determine positive improvement in HPV knowledge in young student populations. Taking into account the young age of the target population (9–13 year old), educational HPV strategies, usually, are tailored to provide parents' engagement and education rather than students. However, parents could often be uncomfortable in the discussion of HPV prevention and sexual-related issues with their children. Therefore, young and older students who receive the vaccination, in a passive way, have low awareness and knowledge about the HPV virus.[41] This study will provide insights into this research area, with

particular attention to the proposal of an innovative integrated approach of PPI activities and multi-disciplinary team input, from the co-design of the educational strategy and contents to the dissemination of the results, including several stakeholders, such as teachers, students, parents, and health-care professionals. Some important limits also need to be highlighted. Firstly, the uncontrolled pre-post test design could affect the internal validity of the study. However, recently, quasi-experimental designs have been broadly applied to test and evaluate the impacts of different interventions on vaccine uptake, by considering the selection of the study design also depending on the outcomes measured, the availability of data and controls, and the way of the implementation of interventions.[42] Based on these considerations, it is important to point out that an uncontrolled pre-post test design allows to evaluate the effect of the intervention in a real-world setting by considering the organizational variables of the schools that, in our context, do not allow a random allocation of the intervention because of ethical issues as well as practical and logistical constraints.[43]

Secondly, given the self-reported data collection approach, recall bias and unintentional misrepresentation of students' vaccination status by parents, will be considered and discussed. Therefore, in order to limit this bias, we used a PPI approach able to improve the awareness of adolescents and their parents about the HPV vaccination. Finally, we will conduct a study in a limited geographical area, and this has the potential to impair the representativeness of the sample. However, we will test the effectiveness of a specific type of educational intervention and, if positive outcomes will be found at the end of the study, the same method should be replicated by extending it to larger populations.

Cost-prevision of the project

Any costs of consumables, training meetings aimed at standardizing the behaviors and procedures to be implemented by all health-care professionals, which afferent to the Data Collection Center regarding study procedures, will be shared by the Coordinating Center and collaborating centers. Spaces for dissemination interventions will be provided by the member schools.

Dissemination policy

The results of this study protocol will be published in appropriate and relevant peer-reviewed journals, to ensure findings sharing with health-care professionals and academics. Moreover, data from this study will be presented at national and/or international conferences or at other appropriate scientific events, as well as presented to stakeholders including the local health authorities and school officials to discuss possible cooperation and development for further implementation of the educational intervention. Furthermore, an internet channel for the research project will be implemented for the online dissemination of the main results to the public, potential users, media, and other researchers.

Ethics approval and consent to participate

The study was approved by the Ethics Committee "Comitato Etico Indipendente – AOU "Consorziale Policlinico" of Bari with the following approval number: 2023–7581/0015620|16/02/2023. The study will be carried out in accordance with the principles of the Declaration of Helsinki and other relevant regulations. Study participation will be voluntary, and signed informed consent will be obtained from participants.

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Authors' contributions

Marco Tomietto, Valentina Simonetti, Dania Comparcini, Giancarlo Cicolini: Conceptualization, Methodology. Marco Tomietto, Valentina Simonetti, Dania Comparcini, Pasquale Stefanizzi, Francesco Pastore, Giancarlo Cicolini: Data curation, Writing and Original draft preparation. Marco Tomietto, Valentina Simonetti, Dania Comparcini, Silvio Tafuri, Giancarlo Cicolini: Supervision. Marco Tomietto, Valentina Simonetti, Dania Comparcini, Silvio Tafuri, Giancarlo Cicolini: Writing, Reviewing and Editing.

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Data availability statement

This protocol does not report results. The identified research data will be made publicly available when the study is completed and published.

References

1. Centers for Disease Control and Prevention. STD Facts - Human papillomavirus (HPV). [accessed 2023 Jul 28]. https://www.cdc.gov/std/hpv/stdfact-hpv.htm.
2. Lurie S, Mizrachi Y, Chodick G, Katz R, Schejter E. Impact of quadrivalent human papillomavirus vaccine on genital warts in an opportunistic vaccination structure. Gynecol Oncol. 2017;146(2):299–304. doi:10.1016/j.ygyno.2017.06.001.
3. Mennini FS, Fabiano G, Favato G, Sciattella P, Bonanni P, Pinto C, Marcellusi A. Economic burden of HPV9-related diseases: a real-world cost analysis from Italy. Eur J Health Econ. 2019;20(6):829–840. doi:10.1007/s10198-019-01044-3.
4. Brisson M, Kim JJ, Canfell K, Drolet M, Gingras G, Burger EA, Martin D, Simms KT, Bénard É, Boily MC. et al. Impact of HPV vaccination and cervical screening on cervical cancer elimination:

a comparative modelling analysis in 78 low-income and lower-middle-income countries. Lancet. 2020;395 (10224):575–590. doi:10.1016/S0140-6736(20)30068-4.
5. Kirby T. FDA approves new upgraded Gardasil 9. Lancet Oncol. 2015;16(2):e56. doi:10.1016/S1470-2045(14)71191-X.
6. World Health Organization (WHO). Major milestone reached as 100 countries have introduced HPV vaccine into national schedule. [accessed 2023 Jul 28]. https://www.who.int/news/item/31-10-2019-major-milestone-reached-as-100-countries-have-introduced-hpv-vaccine-into-national-schedule.
7. Schiller JT, Lowy DR. Raising expectations for subunit vaccine. J Infect Dis. 2015;211(9):1373–1375. doi:10.1093/infdis/jiu648.
8. Bianchi FP, Gallone MS, Fortunato F, Boccalini S, Martinelli D, Prato R, Tafuri S. Epidemiology and cost of cervical cancer care and prevention in Apulia (Italy), 2007/2016. Ann Ig. 2018;30 (6):490–501. doi:10.7416/ai.2018.2249.
9. Ministry of Health. National prevention plan 2014-2018. [accessed 2023 May 13]. https://www.salute.gov.it/portale/news/p3_2_1_1_1.jsp?menu=notizie&id=1908.
10. World Health Organization. Human Papillomavirus (HPV) vaccination coverage. [accessed 2023 Jun 28]. https://immunizationdata.who.int/pages/coverage/hpv.html?CODE=ITA&YEAR=.
11. Ministry of Health [Ministero della Salute]. Commento alle coperture vaccinali al 31.12.2020 per HPV. [accessed 2024 Jan 8]. https://www.quotidianosanita.it/allegati/allegato660418.pdf.
12. Wolff E, Elfström KM, Haugen Cange H, Larsson S, Englund H, Sparén P, Roth A. Cost-effectiveness of sex-neutral HPV-vaccination in Sweden, accounting for herd-immunity and sexual behaviour. Vaccine. 2018;36(34):5160–5165. doi:10.1016/j.vaccine.2018.07.018.
13. Prue G. Vaccinate boys as well as girls against HPV: it works, and it may be cost effective. BMJ. 2014;349:g4834. doi:10.1136/bmj.g4834.
14. Marcellusi A, Capone A, Favato G, Mennini FS, Baio G, Haeussler K, Bononi M, HPV Italian Collaborative Study Group. Health utilities lost and risk factors associated with HPV-induced diseases in men and women: the HPV Italian collaborative study group. Clin Ther. 2015;37(1):156–167.e4. doi:10.1016/j.clinthera.2014.11.002.
15. Gottvall M, Tydén T, Höglund AT, Larsson M. Knowledge of human papillomavirus among high school students can be increased by an educational intervention. Int J STD AIDS. 2010;21(8):558–562. doi:10.1258/ijsa.2010.010063.
16. Italian National Institute of Health [Istituto Superiore di Sanità]. Strategie vaccinali nazionali e regionali per la vaccinazione anti-HPV e primi dati di copertura vaccinale: a che punto siamo. [accessed 2024 Jan 8]. https://www.epicentro.iss.it/ben/2010/novembre/2.
17. Marek E, Dergez T, Rebek-Nagy G, Szilard I, Kiss I, Ember I, Gocze P, D'Cruz G. Effect of an educational intervention on Hungarian adolescents' awareness, beliefs and attitudes on the prevention of cervical cancer. Vaccine. 2012;30(48):6824–6832. doi:10.1016/j.vaccine.2012.09.012.
18. Chandeying N, Thongseiratch T. Systematic review and meta-analysis comparing educational and reminder digital interventions for promoting HPV vaccination uptake. NPJ Digit Med. 2023;6(1):162. doi:10.1038/s41746-023-00912-w.
19. Arghittu A, Dettori M, Dempsey E, Deiana G, Angelini C, Bechini A, Bertoni C, Boccalini S, Bonanni P, Cinquetti S. et al. Health communication in COVID-19 era: experiences from the Italian VaccinarSì network websites. Int J Envir Res Pub Health. 2021;18(11):5642. doi:10.3390/ijerph18115642.
20. Fisher H, Audrey S, Chantler T, Finn A, Letley L, Mounier-Jack S, Thomas C, Yates J, Hickman M. Co-production of an educational package for the universal Human Papillomavirus (HPV) vaccination programme tailored for schools with low uptake: a participatory study protocol. BMJ Open. 2020;10(11):e039029. doi:10.1136/bmjopen-2020-039029.
21. Fisher H, Hickman M, Ferrie J, Evans K, Bell M, Yates J, Roderick M, Reynolds R, MacLeod J, Audrey S. Impact of new consent procedures on uptake of the schools-based human papillomavirus (HPV) vaccination programme. J Public Health. 2022;44(1):199–206. doi:10.1093/pubmed/fdaa164.
22. Kline RB. Principles and practice of structural equation modeling. New York: The Guilford Press; 2005.
23. Istituto Nazionale di Statistica (ISTAT). Popolazione residente. [accessed 2023 March 13]. https://demo.istat.it/app/?i=POS.
24. Faul F, Erdfelder E, Lang A-G, Buchner A. G*power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. Behav Res Methods. 2007;39(2):175–191. doi:10.3758/bf03193146.
25. Forster AS, McBride KA, Davies C, Stoney T, Marshall H, McGeechan K, Cooper SC, Skinner SR. Development and validation of measures to evaluate adolescents' knowledge about Human Papillomavirus (HPV), involvement in HPV vaccine decision-making, self-efficacy to receive the vaccine and fear and anxiety. Pub Health. 2017;147:77–83. doi:10.1016/j.puhe.2017.02.006.
26. Olarewaju VO, Jafflin K, Deml MJ, Zimmermann C, Sonderegger J, Preda T, Staub H, Kwiatkowski M, Kloetzer A, Huber BM. et al. Application of the Parent Attitudes about Childhood Vaccines (PACV) survey in three national languages in Switzerland: exploratory factor analysis and Mokken scale analysis. Hum Vaccin Immunother. 2021;17(8):2652–2660. doi:10.1080/21645515.2021.1894894.
27. Opel DJ, Taylor JA, Mangione-Smith R, Solomon C, Zhao C, Catz S, Martin D. Validity and reliability of a survey to identify vaccine-hesitant parents. Vaccine. 2011;29(38):6598–6605. doi:10.1016/j.vaccine.2011.06.115.
28. Opel DJ, Mangione-Smith R, Taylor JA, Korfiatis C, Wiese C, Catz S, Martin DP. Development of a survey to identify vaccine-hesitant parents: the parent attitudes about childhood vaccines survey. Hum Vaccin. 2011;7(4):419–425. doi:10.4161/hv.7.4.14120.
29. Opel DJ, Taylor JA, Zhou C, Catz S, Myaing M, Mangione-Smith R. The relationship between parent attitudes about childhood vaccines survey scores and future child immunization status: a validation study. JAMA Pediatr. 2013;167(11):1065–1071. doi:10.1001/jamapediatrics.2013.2483.
30. Corporation S. Stata base reference manual: release 12. College Station, TX: StataCorp; 2011.
31. Weber SB. An effective way to detect outliers in multivariate data using Stata (and mata). Stata J. 2010;10(3):331–8. doi:10.1177/1536867X1001000302.
32. Graham JW. Missing data analysis: making it work in the real world. Annu Rev Psychol. 2009;60(1):549–76. doi:10.1146/annurev.psych.58.110405.085530.
33. Enomoto R, Hanusz Z, Hara A, Seo T. Multivariate normality test using normalizing transformation for Mardia's multivariate kurtosis. Commun Stat Simul Comput. 2020;49(3):684–698. doi:10.1080/03610918.2019.1661476.
34. Devellis RF. Scale development: theory and applications. 4th ed. Thousand Oaks (CA): Sage Publications; 2017.
35. Regulation (EU) 2016/679 of the European Parliament and of the council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing directive 95/46/EC (General data protection Regulation). 2016. OJ L 119/1.
36. Chan AW, Tetzlaff JM, Altman DG, Laupacis A, Gøtzsche PC, Krleža-Jerić K, Hróbjartsson A, Mann H, Dickersin K, Berlin JA. et al. SPIRIT 2013 statement: defining standard protocol items for clinical trials. Ann Intern Med. 2013;158(3):200–207. doi:10.7326/0003-4819-158-3-201302050-00583.
37. Aiyegbusi OL, McMullan C, Hughes SE, Turner GM, Subramanian A, Hotham R, Davies EH, Frost C, Alder Y, Agyen L. et al. Considerations for patient and public involvement and engagement in health research. Nat Med. 2023;29 (8):1922–1929. doi:10.1038/s41591-023-02445-x.
38. National Institute for Health Research. Patient and public involvement in health and social care research. A handbook for researchers.

[accessed 2024 Jan 11]. https://www.rds-yh.nihr.ac.uk/wp-content/uploads/2015/01/RDS_PPI-Handbook_2014-v8-FINAL-11.pdf.
39. Karafillakis E, Peretti-Watel P, Verger P, Chantler T, Larson HJ. The role of maturity in adolescent decision-making around HPV vaccination in France. Vaccine. 2021;39(40):5741–5747. doi:10.1016/j.vaccine.2021.08.096.
40. Audrey S, Farr M, Roderick M, Evans K, Fisher H. How acceptable is adolescent self-consent for the HPV vaccination: findings from a qualitative study in south-west England. Vaccine. 2020;38(47):7472–7478. doi:10.1016/j.vaccine.2020.09.074.
41. Flood T, Wilson IM, Prue G, McLaughlin M, Hughes CM. Impact of school-based educational interventions in middle adolescent populations (15–17yrs) on Human Papillomavirus (HPV) vaccination uptake and perceptions/knowledge of HPV and its associated cancers: a systematic review. Prev Med. 2020;139:106168. doi:10.1016/j.ypmed.2020.106168.
42. Lopez Bernal JA, Andrews N, Amirthalingam G. The use of quasi-experimental designs for vaccine evaluation. Clin Infect Dis. 2019;68(10):1769–1776. doi:10.1093/cid/ciy906.
43. Handley MA, Lyles CR, McCulloch C, Cattamanchi A. Selecting and improving quasi-experimental designs in effectiveness and implementation research. Annu Rev Public Health. 2018;39(1):5–25. doi:10.1146/annurev-publhealth-040617-014128.